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THE MEDICAL CLINICS
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NORTH AMERICA

Volume 10 No. 2

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DIAGNOSIS AND TREATMENT OF ACUTE AND CHRONIC MYOCARDIAL WEAKNESS[1]

THE subject I have chosen deals with phases of medicine that confront every practitioner every day, for the crises of disease are practically all dominated by the strength or weakness of the circulation. By the response of the heart and its branches, the blood-vessels, the sick stand or fall. Simple as this statement is, the problems involved are far from simple.

When we say a pneumonia patient died because his heart gave out it seems trite, but when we come to analyze what has actually happened we find ourselves at once in a maze difficult to thread. If tonight I attempt to imitate Ariadne, I do so with proper distrust of my powers. After I have discussed the acute phases of circulatory failure I shall take up the chronic ones which have a character somewhat different.

I have spoken of pneumonia—let me use that disease as a text. I might with equal propriety choose typhoid fever, influenza, or septicemia.

A patient with acute lobar pneumonia presents the signs and symptoms of a severe toxemia—his temperature is high, the pulse rapid, the heart sounds, especially the second pulmonic, feeble; the blood-pressure has fallen from 120 to 100 systolic, and the diastolic pressure is low.

[1] Address delivered before the William Pierson Medical Library Association, Morristown, N. J., March 9, 1926.

The hitherto healthy lung shows a number of moist râles, the skin is a little leaky, the abdomen distended with gas, and the diaphragm pushed up. The sleepless patient is beginning to be delirious. Everything points to a grave situation; we realize that the patient may succumb before a favorable crisis has had a chance to occur. Death, if it ensues, is attributed to failure of the circulation.

What has happened? The poison of the disease, the pneumotoxin, and, as I believe, the metabolic poisons derived from the cellular exudate in the diseased lung, have caused a degenerative change in the heart muscle and in the muscle tissue of the blood-vessels, probably also in the vasomotor mechanism, central and peripheral; likewise in the capillary circulation in all organs and tissues. Other factors, obscure and subtle, may contribute to the process—changes in the endocrine glands to which in acute diseases little attention has so far been given.[1]

The result of the conjoint action of these various factors is a weakening of the heart's action, a fall in blood-pressure, and generalized pulmonary edema. What we call heart failure in acute disease (and after operation) is, therefore, a widespread complex process about which we have very much to learn.

Whether the condition proves fatal or not depends to some extent upon what we do—before and during the danger period—to a larger extent upon the forces of resistance, innate and newborn, in the patient.

Treatment.—I shall divide this phase of the subject into two parts: (*a*) anticipatory or prophylactic, (*b*) curative.

(*a*) *Anticipatory.*—Knowing what may happen, we must do everything in our power to spare the patient both physical and psychic disturbance, make the environment quiet, keep away visitors, move the patient as little as possible, making examinations only when essential, and then quickly; secure abundant sleep by means of opiates, and give a proper diet—milk or butter-

[1] The work of Müller and Petersen (Klin. Woch., January 8, 1926), on what they term "splanchnoperipheric equilibrium," promises to throw some light on this field.

milk, cereals, broth, junket, water-ice, orange-juice, egg albumen, water in abundance or at least sufficient to secure an output of from 1500 to 1800 c.c. of urine. The bowels are kept open with a gentle laxative—milk of magnesia, phenolphthalein, or cascara, or by means of an enema on alternate days. If the pulse is over 100 small doses of digitalis may be given, 5 to 10 drops every six hours.

I shall not enter into the controversy as to whether digitalis is or is not of value in acute fevers. It may be said, however, that one rarely finds the pulse reduced under its use. Since Plummer has shown the harmfulness of the drug as a routine measure in exophthalmic goiter prior to operation, men generally have been thinking about the value of digitalis in other conditions. Formerly I employed it routinely in all cases of pneumonia regardless of the pulse rate. However, I have come to the conviction that when the pulse is slow—in the neighborhood of 90—digitalis is not indicated; but when the pulse is 100 or higher then it ought to be used.

(*b*) *Curative.*—The conditions that chiefly confront us during the critical period of the disease are: (1) vasomotor paralysis, (2) weakness of the heart's action, (3) pulmonary edema, possibly consequential to the other two.

The first, that is, vasomotor paralysis, is best controlled by the use of pituitrin hypodermically—from $\frac{1}{2}$ to 1 ampule of surgical pituitrin every six hours. For the second, one or more of the well-known cardiac stimulants may be used: caffein-sodium benzoate, camphor in oil, digitalis, whisky. And for the third, atropin sulphate in large doses. If the patient is very cyanotic venesection may prove of value.

It is probable that glucose acts as a muscle food, and hence it is advisable to administer it freely in cases of acute myocardial weakness. It may be given in the form of a 5 or 10 per cent. solution by bowel or intravenously.

Should the patient be very restless or sleepless, a small dose of morphin is the best remedy. It acts under such conditions not only as a sedative, but as a veritable cardiac stimulant.

CHRONIC FAILURE OF CIRCULATION

Leaving out of consideration such episodal phenomena as angina pectoris, coronary thrombosis, and rupture of the heart, chronic cardiac disease, when it begins to manifest itself, gives rise to a great variety of symptoms among which the respiratory and gastro-intestinal are the most conspicuous.

When we try to analyze the clinical picture we find it difficult to determine to what partitional extent the heart muscle, the valvular defect, and the vessels contribute to the totality of the picture. Certain it is that a valvular defect can exist for many years without signs or symptoms of cardiac impairment. Eventually, through increasing inadequacy of the intracardiac circulation, the hypertrophied muscle begins to weaken and then conditions are ripe for the development of symptoms.

Some have carried the thought of the part played by the heart muscle too far and have made light of murmurs, especially of that of mitral insufficiency; and yet the valvular lesion if old must be looked upon as the starting-point of subsequent, even if long-delayed, myocardial inadequacy It is, however, true—as the experience of men in large hospitals proves—that the self-same decompensatory process can occur in hearts without valvular defect Here the cause must be a muscle degeneration or fibrosis. This particular type—we might call it the non-valvular type of myocardial disease—is related to hypertension or to disease of the intrinsic vessels through which the nutrition or proper metabolism of the heart muscle suffers

A cursory autopsy often fails to show an adequate reason for the failure of the heart so evident during life, there being no marked signs of fibrosis, no adherent pericardium, no coronary disease, and no striking degeneration. While the microscope may sometimes reveal changes in the muscle-fibers or in the conducting mechanism of the heart, the changes are often too slight to explain the symptoms of heart failure so evident before death.

The reverse is also true, and one may find in persons dying of accidental causes advanced myocardial or coronary disease, or both—although there were no symptoms of cardiac weakness during life.

There is but one conclusion to be drawn trom these facts, namely, that cardiac adequacy and cardiac inadequacy are in the last analysis matters of function, and that anatomic structure, as far as our present methods of study go, is not a reliable index of functional capacity. Much additional light is needed on this subject. It may come from biochemistry and from a better knowledge concerning capillary circulation and the permeability of the endothelial cells.

It is a common practice in certain Philadelphia hospitals to use the term "chronic myocarditis" in non-valvular cases of heart failure. When I use the term "non-valvular," I do not necessarily mean "murmurless"—a mitral systolic murmur or an aortic systolic murmur is often present. By "non-valvular" I mean non-endocarditic—the disease of the heart wall, whatever it be, depending on something else than a valvular defect. The mitral systolic murmur just mentioned is often a functional or dynamic murmur due to cardiac dilatation, and the murmur heard at the aortic area in this same type of case is due to sclerosis of the aortic arch rather than to disease of the aortic valve.

Whether it is right and proper to use the term "chronic myocarditis" in such cases is still a controversial question. As I have indicated above, in some cases no evidence of inflammation is found. A somewhat similar situation exists with regard to the kidneys and has led to the use of the terms "nephrosis" and "nephritis" to indicate non-inflammatory and inflammatory disease of the kidneys. Accepting that as a guide, I have coined the word "myocardosis" to cover those cases of chronic myocardial failure in which the signs of inflammation are lacking.

The pathogenesis of chronic myocardial failure is by no means well understood. Syphilis may play a part, but it is not nearly so important as some writers would make us believe. Nevertheless, the interesting studies of Warthin call attention to the fact that lues may exist when it is not suspected.

Heredity—the inheritance of less resistant tissues—is a very important factor often revealed if a careful family history is taken. Mental and physical strain, focal infections in various distant parts, particularly in the gall-bladder, disease of the

thyroid gland (toxic goiter), are additional etiologic factors. Acute diseases, such as influenza, repeated attacks of pneumonia, may by producing degenerative processes lay the groundwork of chronic myocardial failure appearing years afterward. I have a particular thought in mind in referring to acute diseases as a possible factor in the development of chronic myocardial weakness, namely, that we must give more attention to our patients during convalescence from acute diseases. It is my firm belief that if we would watch the circulation more carefully in patients recovering from acute infections, even as trivial a one as tonsillitis, and also from operations, we should not infrequently find reasons for stepping in to act as guardians of the future. We should find a marked rise in the pulse rate on slight effort, a persistently low blood-pressure, a little shortness of breath, a sense of fatigue on exertion—all indicating a slightly damaged circulation. If neglected nothing may happen for years, then under a strain or in some acute disease of little moment or after an operation the patient begins to show the familiar signs and symptoms of failing circulation. Perhaps then the real cause, dating back many years, is all but forgotten.

To the one who sees in prevention the doctor's greatest usefulness, these things are of signal importance, and justify constant emphasis. Please remember the slogan, "Watch the convalescent."

And now we come to the consideration of the diagnosis of myocardial failure, using the phrase in its widest sense.

When there is dropsy the diagnosis is easy, but the diagnosis ought to be made, for the good of the patient, before dropsy occurs. If there is a valvular murmur, even a cursory examination will fix attention upon the heart, but in the absence of a murmur, if there is no dropsy, many will not realize that the heart is the chief factor in the beginning drama.

What are the more obscure manifestations of circulatory failure in the presence of which diagnostic errors are possible? These are many. I shall mention only the most important:

Symptoms.—*Cough.*—Spasmodic or continuous cough, severe or mild in nature, may be the chief if not the only symptom

of a weakening heart. It is instructive to see how useless the ordinary cough medicines are in such cases. Opiates help, but they do not cure. Only rest and digitalis will do that. I shall defer a discussion of the means of diagnosis until I have spoken of some other symptoms.

Gastro-intestinal Symptoms.—These are pain, gaseous distention, flatulence, loss of appetite, at times pronounced nausea and even vomiting, but often merely a sense of pressure in the lower chest or epigastrium. The feeling of gaseous distention or of pressure may come only on effort, and as it is quickly relieved by the eructation of gas, the patient is quite convinced that the fault lies in his stomach. The doctor who fails to penetrate beneath the surface of things often will share that conviction. Patients have died suddenly who have never had anything more to complain of than a sense of oppression in the lower chest and epigastrium. In the newspapers such cases are often attributed to "acute indigestion"—a journalistic diagnosis based on error.

Shortness of Breath.—This is usually an early manifestation, but is not of necessity present. The others I have mentioned may overshadow it. The diagnosis of the real cause is less difficult, for dyspnea is associated in every physician's mind either with some disease of the lungs or with disease of the heart. While the doctor may correctly attribute the shortness of breath to the heart, it frequently happens that he overlooks the most important factor in the dyspnea, viz., a hydrothorax. The frequency with which I find an unsuspected pleural effusion I rate as one of the most remarkable experiences in my work as a clinician. No skill is required to discover this apart from a thorough routine examination and the ever-present thought that persistent shortness of breath is likely to be dependent on some additional factor.

Ascites as a monosymptomatic occurrence, *i. e.*, one unaccompanied by such symptoms as general anasarca, fever, pain, etc., is a difficult nut for the diagnostician to crack. It may be due to tuberculous peritonitis, to abdominal or pelvic carcinoma, to cirrhosis of the liver, and these will be the first thoughts entertained. Few men, unless they have had experience with this

condition, will think of the heart as the cause of such a silent ascites as I am in the habit of terming it. Nevertheless, that is an ever-present possibility. As regards the cardiac lesion underlying the ascites, it may be an adherent pericardium (Concato's or Pick's disease) or it may be nothing more than a dilatation of the heart and myocardial relaxation. A satisfactory explanation is wholly wanting why the latter condition in rare circumstances produces an ascites instead of a general dropsy.

Enlargement of the Liver.—This in cardiac decompensation commonly effects the right lobe or both lobes, so that the organ projects for a greater or lesser distance below the right costal arch and enters the epigastric triangle. There are, then, no great diagnostic difficulties. Sometimes, however, the left lobe bears the chief brunt of the process of passive congestion, forming a conspicuous swelling in the epigastrium. This peculiar enlargement, more frequent perhaps in mitral stenosis than in other cardiac lesions, is easily interpreted as a new growth of the stomach or liver. If vomiting and anorexia are present, this belief will naturally be strengthened. A careful analysis of the history and a painstaking physical examination are the only ways in which errors can be avoided.

Acute Recurrent Pulmonary Edema.—This catastrophic symptom is perhaps most common in cases of hypertension, especially in those of nephritic origin, but it is also seen in myocardial disease with or without valvular lesions and with or without increase in blood-pressure. The pathogenesis of this condition which I have discussed elsewhere is obscure.[1] When hypertension exists we feel that there is an adequate explanation, although we really do not quite understand what happens, but in the absence of hypertension and in the absence of a valvular lesion the fact that the sudden pulmonary edema is really of cardiac origin may not be suspected.

Psychoses.—The last symptom I should like to mention in my survey of the phenomena caused by circulatory weakness or failure is mental disturbance. It may happen during the course

[1] Acute Pulmonary Edema with Special Reference to a Recurrent Form' Amer. Jour. Med. Sci., January, 1907.

of decompensation that a patient develops a mania-like psychosis or a delusion or a fear of poisoning. The phases are manifold and perplexing, and often suggest a primary insanity. However, they are really secondary, and are due to disturbance of the cerebral circulation or, in rare instances, to a toxic effect of digitalis.

Diagnosis.—I now come to a consideration of those signs by which myocardial weakness may be discovered, especially in what might be called "larval cases." One of the best means, in my opinion, is to determine the cardiac outline. This can be readily accomplished by locating the heart beat through inspection and palpation and by outlining the boundaries of the heart by light percussion.[1]

These methods are more important in many cases than auscultation, not that auscultation is a negligible procedure—far from it—but it may mislead, while inspection, palpation, and percussion rarely do so. I have said that auscultation may mislead; this statement requires some explanation. Myocardial failure may exist with perfect rhythm and with what are to all intents and purposes normal heart sounds. Nevertheless, in such cases the other methods of physical diagnosis will show changes.

As I said earlier in this paper, a systolic murmur at the mitral area or at the aortic area may be revealed on auscultation. These are more or less accidental and are not due to endocardial changes. Auscultation may also show arhythmias; these, however, are often of little diagnostic value as regards the nature of the case, and certainly not as regards its gravity. For example, one may find auricular fibrillation in a heart with entire functional capacity. Much might be said, however, upon the subject of arhythmia in connection with myocardial disease, but this would carry me too far afield. A gallop rhythm of a certain type should, however, be mentioned on account of its diagnostic and prognostic importance. It is the one in which the first sound is

[1] Some of my friends advocate heavy percussion, but personally I prefer light percussion, which I find gives good results providing the plexímeter finger is pressed firmly upon the chest.

reduplicated, the so-called anapest type or *bruit de galop.* In the absence of a febrile process it indicates serious cardiac damage. I have found it most frequently in a type of myocardial failure that I would call "progressive myocarditis," using myocarditis in its widest sense. This type is often but not always associated with true nephritis.

The electrocardiograph gives a good deal of information not only regarding the arythmias but also regarding the state of the myocardium, so that when available it should be brought into the case, but it is not essential, and every practitioner can learn to diagnose the important arhythmias or important myocardial changes without it.

Treatment.—The treatment of chronic failure of the circulation is a simple matter as a rule, if the true conditions are recognized—rest in bed, mental rest, light meals, open bowels, and digitalis sum up all of the treatment in the ordinary case. One should bear in mind the frequency of undiscovered pleural effusion. When found, the effusion is removed by tapping. If there is reason to think it has been of long standing, the tapping should be done very slowly so as to guard against the danger of acute pulmonary edema which I have called "edema by recoil." If there is much dropsy, salt restriction is indicated. In the more advanced cases, when there is general dropsy with cyanosis and shortness of breath, digitalis is the mainstay of treatment. The mode of administration, the preparation used, and the individual dose are not so vitally important. Most of the preparations on the market seem to have merit.

When the liver is enlarged, and if there is no evidence of primary kidney disease, then I find the following capsule, a modification of the Niemeyer pill, very useful:

Powdered digitalis	0.06 (gr. 1)
Calomel	0.06 (gr. 1)
Powdered squill	0.06 (gr. 1)
Caffein	0.06 (gr. 1)

It is necessary when giving this to watch for salivation. Diuretics are of value; among the best are theocin and theobromin.

If digitalis fails or is not well borne, good results are sometimes obtained by giving the fluidextract of apocynum cannabinum in doses of from 5 to 8 minims three or four times a day.

For restlessness and insomnia nothing equals a small dose of morphin which, just as in acute cases, acts here too as a cardiac stimulant by its sedative and sleep-producing effects. In cases with chronic cyanosis and distention of the veins, venesection is helpful, particularly when there is marked orthopnea. In cases with cyanosis so profound as to raise a suspicion of mediastinal tumor or coal-tar poisoning, free bleeding from the arm is unequaled as a remedial agent. If the dropsy is unyielding to drugs, scarification of the legs or the use of Southey's tubes not only removes the dropsy, but often restores compensation.

The Nauheim treatment, either on its native heath in western Germany or at home, or in some well-known sanitariums in this country, is useful, especially in cases not associated with hypertension and advanced arterial hardening.

CLINIC OF DRS. JOSEPH SAILER AND
FRANK B. LYNCH

UNIVERSITY HOSPITAL AND PEPPER LABORATORY

BACKACHE IN BLOOD-STREAM INFECTION

BACKACHE may at times be the most puzzling condition that the physician is required to diagnose. The 5 cases that follow present certain common features, and although the actual pathology may vary, it is also possible that they present an especial type of backache.

The first patient is a Russian Jew, obviously with a strong Tartar admixture. He is twenty-nine years of age, and a musician by profession. His previous history consisted of a doubtful attack of renal colic, occasional cardiac palpitation on awakening, and a slight morning expectoration. There had been a few upper respiratory infections in 1925, but no other attacks of sickness. In September he had a pain down the left leg. This grew rapidly worse and he was completely incapacitated; the pain extended to the sacral regions. It was worse if he attempted to play the piano or to walk. It disturbed sleep, and he noted particularly that he could not sleep on the left side. There were no sensory disturbances, except a slight numbness over the distribution of the right external cutaneous nerve (meralgia paresthetica), and tenderness just beneath the left anterior superior spine of the ilium. Vibratory sensation seemed diminished over both patellar tubercles, right 11 sec., left 6 sec., but normal over the anterior superior spines of the ilia. Leaning forward produced a spasm of the lumbar muscles. There were no tender points in the back.

The general physical examination at this time gave normal heart and lungs, a slight splash in the stomach, tremulous eyelids, and normal reflexes. The Wassermann test was negative, the blood-pressure 126/86; urine normal; Hb. 86 per cent., r. b. c., 3,980,000; w. b. c., 6150. Gastric contents, bread and water removed in thirty minutes, gave free hydrochloric acid 45, total acidity 55, no occult blood.

For a month the pain grew steadily worse, and was most severe between 3 and 4 A. M. The paresthesia over the left thigh had disappeared after the application of faradic electricity, and there was no longer tenderness at the left anterior superior spine. The laboratory tests were the same. The teeth and tonsils were normal, and there was no evidence of any other focus. His weight had varied from 113 to 116 pounds. *x*-Ray studies revealed nothing. He consulted other physicians, who found nothing. Therefore in December, 1925 Dr. Lynch, of the Pepper Laboratory, was asked to take a blood-culture. This was positive, and a non-hemolytic streptococcus (Streptococcus mitis—Holman) was obtained, and from this a vaccine was made and administered. The results were satisfactory. In March he was able to resume his work in his usual strenuous manner. On March 31st a second blood-culture was negative.

The second patient is a Russian Jewess, thirty-one years of age, also obviously with Tartar ancestry. She was first seen on November 5, 1925, complaining of "pain all over." Ten years previously, during pregnancy, she had developed pain in the left thigh; four years later, again, during pregnancy, pain had developed in the right thigh. Recently she has had pain in the nates, which is made worse by walking or any exertion. She has also had pain in both arms, numbness and sense of coldness in both index-fingers, and gnawing pain in the right hypochondrium. She is distinctly neurotic. Her previous history excluded severe infectious disease, operations, and injuries. She had had occasional spells of vomiting. She had chronic constipation and used laxatives constantly. She had borne 5 children, 2 of whom had died; menstruation was regular, but

recently had become scanty. The important features of the physical examination were tremulous eyelids, suspicious tonsils, defective dentition, with remaining infected roots, heart and lungs normal, large pits ascribed to chickenpox on the right side of the abdomen. No tenderness in the back or thighs, hyperesthesia of the outer aspects of both thighs, normal reflexes. The blood-pressure was 120/92; the blood, r. b. c. 4,300,000; w. b. c. 5150; hb. 91 per cent.; the urine neutral, sp. gr. 1002, chemically and microscopically normal. An attempt to secure the gastric contents caused vomiting. The vomitus was titrated and gave free hydrochloric acid 20, total acidity 40, no occult blood. The blood-sugar was 103 mg. per 100 of blood taken after breakfast. Diet and alkalies produced no improvement. A second examination gave similar results, and she was induced to enter the medical ward at the Presbyterian Hospital. While there she was examined by a surgeon, a gynecologist, and an orthopedist, all of whom reported normal findings. An *x*-ray study was negative, but Dr. Eiman found in the blood a small non-hemolytic streptococcus growing in the culture-medium in short chains. A vaccine was prepared and given, but the patient reported no relief. She was referred to Dr. George Wilson, who diagnosed psychoneurosis and endocrine imbalance. The basal metabolic test was plus 3.6 per cent.; a second test was uncertain because of restlessness. The patient seems better, but complains as bitterly as ever; a second blood-culture has not been obtained. Fever was not present while the patient was at the hospital.

The third case was a single woman of forty-five, a schoolteacher. She was referred to me by Dr. J. W. Robinson for a severe constant pain in the lower back accompanied by fever and sweating. She had been weak and miserable all winter and incapacitated for six weeks. She felt utterly tired. She had had pleurisy at the age of ten, typhoid fever at twenty. She had not been strong, tiring easily, but had always worked hard, and had been successful. Menstruation had been regular, but profuse. Her weight was $112\frac{1}{4}$ pounds in clothing. Height 5 feet,

$4\frac{1}{4}$ inches. There was no evidence of oral infection, the pulse 108, the temperature variable, reaching 101° F. The examination of the heart indicated a moderate insufficiency of the mitral valve. Inspiratory subcrepitant râles could be heard over the back of the right lung, without evidence of consolidation. There was tenderness with flinching in the lower part of the abdomen, but nothing abnormal could be felt. The rectal examination revealed tenderness of the ischial bones. The laboratory findings were: blood-pressure, 140/88; urine acid, 1026, indican and mucus were present, otherwise normal; blood, r. b. c., 3,750,000, w. b. c. 19,600, Hb. 80 per cent.

She was immediately sent to the University Hospital, where she remained until May 29th. The temperature ranged from 98° to 103° F., gradually declining; the leukocytes decreased from 22,000 to 10,000. Numerous consultations revealed nothing; the *x*-ray was repeatedly negative, although a diagnosis of osteomyelitis had been confidently made; a blood-culture was negative. After the prolonged rest some improvement occurred, and the patient returned to school in the fall. Pain and occasional fever persisted, and on February 1st another blood-culture was taken, and a Streptococcus viridans obtained. A vaccine was prepared and administered, and although the patient presents herself irregularly for inoculation, there has been a distinct improvement.

The fourth case, male, was first seen in January, 1921, at the age of twenty-one, because albumin had been found in his urine when he was examined for life insurance. He had had scarlet fever at seven; no other infections; tonsillectomy at eight; various minor injuries. He was then normal. Albuminuria was not found; the phenolsulphonephthalein test was normal; the electrocardiogram was normal. In March, 1925 he had an attack of vomiting with fever that lasted two days, and since then he had had backache. He was seen three weeks later, but nothing was found; the blood chemistry was normal, the leukocytes were 9000, and the blood-count normal; the gastric acidity was high. The backache became more severe, and was not

affected by fatigue, diet, or the condition of the bowels. He was less uncomfortable in bed. On January 7th a blood-culture was taken, and the Streptococcus ignavus (Holman) was grown. A vaccine was prepared and given, and either as a result of this or coincidentally the backache has ceased. A second blood-culture has not been taken.

The fifth case, a trained nurse, was first seen in 1915, when she complained of pain and stiffness in the joints. She was then twenty-three years of age. She had had pneumonia twice, tonsillectomy, and appendectomy, and at each operation dilatation and curetment had been performed for dysmenorrhea without benefit. Her pain had begun in the sacro-iliac joints, and thence had spread to other joints, but local signs had never been present. There had been daily rise of temperature to about 100° F. The physical examination, except for tenderness over the right sacro-iliac joint, was negative. The leukocytes at this time were 18,400; polymorphonuclear cells 75 per cent. The gastric contents indicated hypersecretion and some retention. Her weight was 105 pounds. She did not improve on various forms of treatment. No focus was found, although repeatedly sought. From time to time she vomited, usually following attacks of pain in the abdomen. Her pulse averaged about 120. Later the stomach contents indicated hyposecretion, and she was given hydrochloric acid. Her general condition improved, but she had headaches. A blowing systolic murmur was sometimes heard. The leukocytes decreased to 7800; polymorphonuclear cells 63 per cent. Tubercle bacilli were never found. Quinin was given for some time, although plasmodia were also absent. Her condition continued about the same, and despite her discomfort, she continued at work. The joint pains gradually disappeared; the headaches became more severe; the temperature persisted. During several holidays she gained weight. At one period she had glycosuria, always, however, with a low blood-sugar. There was no essential change for eleven years. On January 30, 1926 a blood-culture was taken, and the Streptococcus ignavus (Holman) found. I can only

regret that it had not occurred to me to have this done sooner. A vaccine was prepared, but lost. A second vaccine has been prepared, and is now being administered, with at least subjective improvement and a slight gain in weight.

These 5 cases present the common symptom of backache and pains in the legs. One (2) was under prolonged observation in the hospital and never had fever or leukocytosis. Two (1 and 4) were office patients. The temperature was taken only occasionally, and was always normal, and neither had leukocytosis. Two (3 and 5) had fever and leukocytosis, and one of these has had the same symptoms varying slightly for eleven years.

The study of these cases has been incomplete. Only 2 patients have had two blood-cultures, but all have been studied carefully for foci of infection, and although they have not been found, it must, I think, be assumed that they exist. It is conceivable that there has been no blood-stream infection, and that in all or some of the cases contamination occurred after the blood was withdrawn from the body. The most important points in favor of this view are the absence of fever and leukocytosis in these cases (1, 2, and 4). Against it are first, the work was done under favorable conditions in well-equipped laboratories; second, the types of organisms found, not types that usually occur as a result of accidental contamination; third, the fact that there were two bacteriologists working independently, although I should require no confirmation for the work of either; fourth, the apparent recovery or marked improvement that occurred in 2 cases (1 and 4) as a result of autogenous bacterin treatment. I would not place much stress upon this, for such treatment lacks the certainty of result that makes it possible to use it as a proof, or even as confirmatory of other evidence.

Assuming, however, that these observations may be accurate, it will be interesting to consider what conclusions may be drawn from them. That backache may be present in blood-stream infection is not new, but that it may be the only symptom of such an infection is new to me, nor have I been able to discover any allusion to it in a rather cursory search of the litera-

ture. It is even more surprising to me to think of blood-stream infections existing without fever or leukocytosis. Libman has reported such a case with Streptococcus viridans infection. A more remarkable paper was read before the Association of American Physicians in 1915, by Oille, Graham, and Detweiler,[1] in which they reported 26 cases of various conditions, all with a non-hemolytic streptococcic bacteremia, usually the Streptococcus viridans. "None of the series is characterized by progressive emaciation, weakness, and anemia." "Most of the patients look perfectly well, feel well, and had no anemia." "The characteristic temperature appears to be an irregular one, normal all day, often for some days at a time, yet reaching 99° or 99.5° F. two or three days a week at irregular times of the day. To detect this the temperature must be taken systematically for considerable periods of time."

A later report was made of these cases in 1921, and 20 were at that time still alive. All that had lacked them at first had by that time developed heart murmurs, confirming the original impression that they were all cases originally of endocarditis.

As this paper is written particularly with reference to the symptom of backache, I have noted, in the necessarily brief clinical reports, the number of cases in which pain in the back is mentioned. It is mentioned only twice, Cases III and IV. Backache cannot, therefore, be considered as a characteristic symptom of blood-stream infection.

One of the most important problems that still remains unsolved is the cause of acute rheumatic fever, and the relation of this cause to endocarditis. The studies of Swift and of Libman are most important. The heart is involved early in rheumatic fever, and in subacute endocarditis the blood-cultures, in the majority of cases, yield an anhemolytic streptococcus. This does not necessarily prove that this organism is the cause of the endocarditis, although the presumption is very strong, much stronger, for example, than the evidence that the diphtheroid bacillus is the cause of Hodgkin's disease.

[1] Trans. of the Assoc. of Amer. Phys., xxx, 1915, p. 674; Ibid., xxxix, 1924, pp. 226, 260.

There can be little doubt that blood-stream infection with the anhemolytic streptococcus may continue for a long time and is compatible with a moderate degree of comfort. In spite of Libman's statements, and the evidence of Oille, Graham, and Detweiler, the impression exists that a positive blood-culture is exceedingly grave, and, unfortunately, this impression, I believe, is responsible for the fact that blood-cultures are rarely taken except in grave cases.

Report on Bacteriologic Study of Blood.—Mr. L. O., Mr. J. M. A., Mr. H. M. B., Miss M. L., and Miss E. E.

Blood was drawn in each instance by the method described by Fox and Leaman for massive blood-culture as follows: A 400-c.c. wide-mouth bottle is fitted with a rubber stopper having two holes, through each of which passes a piece of glass tubing, one of which has a rubber tubing connection for the needle and the other for suction by the operator. The latter connection has a glass mouth-piece plugged with cotton to prevent the entrance of air. After placing in the bottle 100 c.c. of distilled water containing 2 grams of sodium citrate, the apparatus is assembled, wrapped in muslin, and sterilized for thirty minutes at 15 pounds pressure.

When ready to use, the muslin wrapper is removed and a freshly sterilized needle attached, care being taken that all connections are tight.

The arm is prepared by means of alcohol and tincture of iodin, a tourniquet applied to the arm, and 100 c.c. of blood is drawn into the bottle in the usual manner, suction being made to facilitate the flow. (It is convenient to mark the outside of the bottle with a wax pencil to indicate the level at which the mixture will stand when approximately 100 c.c. of blood has been drawn.)

After the collection the blood citrate mixture is poured, under strict aseptic precautions, into sterile centrifuge tubes and centrifuged at high speed for twenty minutes. The supernatant fluid is poured or pipetted off, and the sediment is cultured in plain and glucose broth, agar-poured plates, deep tube agar and deep serum water brain media, containing 0.5 per cent. glucose.

In all this group of cases in which a growth has been obtained it has grown very slowly, appearing between five and ten days, and taking several days to produce sufficient growth for vaccine preparation. In all cases the organism has been recovered from aërobic cultures, and there has been no growth anaërobically in any case.

The results of culture were as follows:

December, 1925: Mr. L. O.—Non-hemolytic streptococcus (Streptococcus mitis—Holman).

March 31, 1926: Mr. L. O. (after treatment)—Negative.

January 7, 1926: Mr. J. M. A.—Non-hemolytic streptococcus (Streptococcus ignavus—Holman).

February 1, 1926: Miss M. L.—Streptococcus viridans.

Miss E. E. (first culture)—Negative except for contaminating growth of Staphylococcus albus.

Miss E. E. (second culture)—Non-hemolytic streptococcus (Streptococcus ignavus—Holman).

CLINIC OF DR. JOHN H. STOKES

UNIVERSITY OF PENNSYLVANIA

CASE I. THE DIFFERENTIAL DIAGNOSIS OF PSORIASIS AND SYPHILIS

CASE II. THE TREATMENT OF LUPUS VULGARIS, WITH SPECIAL REFERENCE TO THE MISUSE OF *x*-RAY AND RADIUM

CASE III. THE DIAGNOSIS OF DISSEMINATE ERYTHEMATOUS LUPUS

CASE IV. THE PROBLEM OF MALIGNANCY IN THE PRESENCE OF SYPHILIS

SOME days ago a good friend of mine with the viewpoint of the internist in syphilology, gently reproached me with the amount of space to be given to the dermatologic aspects of differential diagnosis of syphilis in a forthcoming publication. A day or two later, a member of my staff commented upon the annoyance of finding a positive blood Wassermann reaction in what he had thought was a plain case of psoriasis. He was inclined to call the technic over-sensitive. And today I present before you, as the background for a little homily on the value of objective differential diagnosis in syphilis, and particularly in cutaneous syphilis, a patient who for a matter of two years has been seen in the clinics of various hospitals, and who finally in my own clinic was diagnosed as having a "psoriasis lichenoides" and presented before a dermatologic society as such with acquiescence of the society in the diagnosis. She has not psoriasis, but syphilis, undiagnosed because of neglect of objective differential criteria, and failure to use them as suspicion-arousers even to the point of taking a blood Wassermann test.

Case I. The Differential Diagnosis of Psoriasis and Syphilis.—Mrs. B. is, as you see, a woman of sixty, bright and alert, with a trenchant wit, and physical handicaps which she

bears with a becoming fortitude. It appears that she has been under the care of an orthopedic clinic for the past two years, wearing a brace part of the time for trouble with her back and hip whose precise nature we could not ascertain, but which has disappeared subsequently under treatment for her syphilitic infection. One of my own staff called the pains in the shoulder and knee of which she complains the arthritis of psoriasis, an association not infrequently observed. Our examination of this patient discloses only a moderate hypertension, a urea-nitrogen of 35 mg., a slight albuminuria. Her major subjective complaint in addition to the bone and skin lesions previously mentioned is obstinate headache. The cutaneous eruption consists of groups of mildly erythematous papules scattered in considerable numbers over the trunk, face, and extremities. Some of the most characteristic lesions appear upon the forehead and the extensor surfaces of the forearms. There is no conspicuous localization to scalp, elbows, and knees. Scaling is not marked—in fact, there is very little of it indeed considering the extent of the eruption and the areas involved. *Configuration*, the arrangement of the individual lesions, always important in differentiation, is evident here. There is a distinctly arciform arrangement in some of the larger groups of lesions. And on the closest inspection, especially in the lesions about the wrist, there is evidence of *atrophy*, almost of slight scarring at what seem to have been the sites of old lesions, now involuted. The mucous membranes are free, the anus and genitalia, too often overlooked in examination, are negative, and the palms and soles show nothing distinctive. The finger-nails, let it be noted, show no pitting or striation such as often occurs in psoriasis.

Following inspection, we proceed to palpate the lesions. To place palpation before inspection—the impulse to "paw" the patient in dermatologic examination, is the earmark of the amateur. On palpation, we find, lightly stroking the lesions with the ball of the middle finger of the right hand, that there is a distinct fleshiness, a firmness to the papule. It "jumps" out from under the finger as it passes across it, and is evidently embedded in the skin, not merely on it.

Arciform configuration, atrophy, and scarring, palpable induration, an extensive distribution without the characteristic localization of psoriasis. Here at once is a galaxy of reasons for not accepting the previous diagnosis of psoriasis, whether of lichenoid or other type. Let me now put before you groups of differential considerations which enable us, irrespective of serologic or other findings, to begin to place this case in its proper category purely on the basis of its cutaneous physical characteristics.

THE TEN BASIC PHYSICAL CHARACTERISTICS OF LATE SYPHILIDS

1. **Solitary Character** or at least the presence of few lesions. This is not invariable.
2. **Asymmetry:** though by no means invariable.
3. **Induration:** deep palpable infiltration.
4. **Indolence:** a relatively low-grade inflammatory process.
5. **Arciform Configuration:** Borders polycyclic or forming segments of circles, both in the individual lesion and in the configuration of a group of lesions.
6. **Sharp Margination of Lesions:** in ulcers, "punched out" appearance.
7. **Tissue Destruction and Replacement:** with or without ulceration.
8. **Tendency to Central or One-sided Healing:** with peripheral extension.
9. **Scar Formation:** superficial *atrophic* (thin and wrinkled), non-contractile. The scar retains the arciform configuration of the original lesions.
10. **Peripheral Hyperpigmentation:** of a rather persistent type.

This must, of course, epitomize all types of late syphilids. But from the group of fundamental signs it is easy to pick at once the cardinal members as applicable to the lesion before us —induration, indolence arciform configuration, atrophy, and scar. And now in contrast let us consider the differential points of psoriasis and its near neighbor, seborrheic dermatitis, in comparison with syphilids.

THE PSORIASIFORM SYPHILID, PSORIASIS, AND SEBORRHEIC DERMATITIS

Syphilid.	*Psoriasis.*	*Seborrheic Dermatitis.*
Common on the face, but less apt to be extensive in the scalp.	Rare on the face, often abundant in the scalp.	Common on the face and scalp. Greasy scale and oily hair, shiny inflamed skin on nose and forehead.
Lesions, papules, or border markedly indurated.	"Resistance" of scale, but no induration.	No induration.
Central atrophy or scarring with peripheral extension.	No atrophy or scar, no matter how severe.	No atrophy, no scar.
No very typical distribution.	Typically appears on scalp, elbows, knees.	Typically appears on scalp, face, presternal and interscapular region.
No capillary hemorrhage from curetted papule.	May get typical capillary hemorrhage from papule.	No capillary hemorrhage.
Scanty friable dirty scale if any.	Scale abundant, silvery, imbricated (not invariable).	Greasy, yellowish fine scale, moderate amount. May be eczematous, oozing, and crusted.

In this differential table one again sees confronting him as characteristic of the syphilid the high points of induration and scar formation. It is not too much to say that upon these major elements in the present eruption, the preliminary diagnosis of a cutaneous syphilid may properly rest.

"But" remarks one of my colleagues, "isn't this too extensive for a syphilid, and especially a late one?" I have many times seen what I call the disseminated recurrence in the skin as extensive as a well-marked urticaria, and confused with one. The so-called neurosyphilid of Unna, is a disseminate recurrence of wide-spread distribution and annular papular type which may at times be taken for psoriasis. This, however, is not an annular syphilid, and arciform configurations, while they suggest syphilis, do not eliminate psoriasis, in which they are often seen. We find ourselves reduced, then, to induration and scar as the earmarks of the syphilid in differentiation from psoriasis. The scar is the product of granulomatous infiltration, which never occurs

in psoriasis. The only psoriasis, so far as I know, that leaves scars or atrophy is that which has been treated with the *x*-ray; and in such a case it, the *x*-ray, and not the psoriasis, leaves the scars, and the atrophy is general over the area of application and not confined to the sites of the lesions. Why hasn't this woman a chronic urticaria? The eruption does not change from day to day or week to week, but only slightly from month to month. The lesions do not come and go, they do not itch, they are too indolent, they leave scars.

We insist, therefore, that a blood Wassermann test be taken, and it is returned strongly and repeatedly positive. Why do I say repeatedly? Because in these days of better comprehension of Wassermann fallibility, all blood Wassermann tests, both positive and negative, should be repeated in the presence of everything but the most obvious clinical confirmation. But suppose the patient has merely a coincident syphilis and a psoriasis? Here the eruption on objective grounds precludes the possibility. Examine critically the lesion you thought was "psoriasis," when a Wassermann report shows syphilis to be present. You will be surprised by the frequency with which you will revise your opinion. Of course the two conditions do co-exist, and when they do, differentiation—and especially induration and atrophy or scar, are the mainstays of diagnosis. In treating these patients, if possible, use mercury or bismuth first, for it is less likely to have a non-specific effect as would an arsenical, upon psoriasis. In this case the renal condition definitely contraindicates intensive mercurialization. Two small doses of neo-arsphenamin will probably produce a 75 per cent. involution of the syphilid, while they would not influence a psoriasis of long standing.[1]

[1] This patient, observed over a period of eighteen months, has under moderately intensive treatment suited to her age and renal tolerance, made a remarkable recovery, including the flare-up (Herxheimer reaction) of the eruption with the early injections, its complete disappearance, the improvement of the nephrosis, and the complete disappearance of the miscellaneous bone and joint symptoms which incapacitated her and made her a wanderer among the surgical and orthopedic clinics of the city.

Case II. The Treatment of Lupus Vulgaris, with Special Reference to the Misuse of *x*-Ray and Radium.—This woman, fifty years of age, developed papules which ulcerated twenty years ago about the nose and face. There was some evidence of a tendency to spontaneous healing, but never a complete involution. As her family physician writes, the lesion was "kept in check" by the use of the *x*-ray, and the patient tells us that she has lost all count of the number of treatments she has had; she thinks there have been "hundreds," over a period of five years. Only in the last six months has there been a striking change, and in this period the lesion has heaped up and become vegetative or cauliflower-like, with marked bleeding on slight trauma. Since this has occurred "intensive" *x*-ray treatment has been used, and she has had an unknown dose every two weeks throughout the six months with little effect.

On examination we find a small, thin woman, with the singularly calm and even pachydermatous manner that one occasionally sees as a happy variation on the usual state of mind of the grossly disfigured person. Her nose is gone, the cartilages and bone of alæ and septum now lost in a rather dry and fortunately almost odorless mass of cauliflower-like vegetations of a greenish-black color, the size of a child's fist. At two points a distinct border may be seen—at the original site of the right ala nasi, and at the point where the mass invades the skin of the forehead. Here one can recognize distinct rolling and pearling. The adjacent skin is free from the miliary tubercles (apple-jelly nodules) usually seen at the periphery of an extending, though less often of a hypertrophic tuberculous process. The patient's general nutritional state and health are fairly good. The *x*-ray examination of the chest shows emphysema and slight old tuberculous involvement of the left upper lobe of the lung. There are no other cutaneous lesions. The blood Wassermann reaction is repeatedly negative.

What enters into the differential diagnosis here? Obviously epitheloma, either primary or secondary to radiotherapy; an hypertrophic syphilid; an hypertrophic lupus vulgaris; one of the rarer granulomas such as blastomycosis and pyogenic (vege-

tative) granulomas which may be papillomatous in structure; and the tropical lesion rare in this part of the world, known as espundia, probably a leishmaniasis. Fungoid lesions such as bromoderma and iododerma are dismissed without critical consideration, and yaws could hardly give such a history.

Carcinoma, of all the lesions which attacks the nose, is the most determined in its attack on bone and cartilage, which have obviously been destroyed wholesale here. It must not be forgotten, however, that the destruction here seen may be the result of the application of an escharotic paste. A lupus vulgaris (tuberculosis) rarely destroys the septum and alæ without leaving at least some involvement of the skin of the cheeks and malar prominences, which is absent here. The age of onset is not too late for tuberculosis, for in my experience tuberculosis of the skin of the face may begin at any age, nor is it too early for carcinoma, for I have seen basal-cell epithelioma on the nasal bridge of a nineteen-year-old girl at the site of eye-glass irritation. The border of the lesion is that of epithelioma, the palate is intact (against espundia), the patient has never left her native state, there is no concomitant or direct evidence of syphilis which, moreover, is much more selective in its activities, and usually causes a collapse of the septum before it removes the nose entire, as in this case. I feel quite sure that we can call this epithelioma, possibly developing on an old tuberculosis or upon an erythematous lupus (which is not tuberculous).

The use of the *x*-ray in the treatment of cutaneous tuberculosis is beginning to receive the condemnation which results from observation of its after-effects. Of all the known types of scar, the scars of burns, and the scars of tuberculosis cutis show the most pronounced tendency to malignant breakdown. Why then, from the standpoint of rational therapeutics, combine the most malignant type of burn scar (that of irradiation) with that of the most dangerous of the granulomas from this particular viewpoint? In other words, *never* treat lupus vulgaris with the *x*-ray. Radium may in a few instances, because of its greater output of soft rays, produce so much surface reaction in so short a time that it will heal the lesion without favoring malignant

change. But never use *x*-ray. In fact we feel confident that had this patient developed her lupus vulgaris now, instead of twenty years ago, the ultraviolet light therapy now so rapidly developing, would have dealt with the situation without such risks. The Kromayer lamp with pressure, systemic irradiation with the air-cooled burner, and perhaps a limited use of the curet and acid nitrate of mercury might have disposed of the lesion in its beginning. It is interesting that the systemic therapy is applicable only to the white patient, for the colored patient shows little response even to enormous doses on account of the high re-radiating power of his pigmented skin. The surgical removal of tuberculous foci in the skin can be brought to a high point of development, likewise, and the non-specific effect of moderate doses of neo-arsphenamin should not be lost sight of. As it is, there is nothing to offer this woman now, but an extensive electrocoagulation, with the outlook one of palliation rather than cure.

Case III. The Diagnosis of Disseminate Erythematous Lupus.—The dermatologist never loses an opportunity to talk about this particular symptom complex (for it should be called such rather than a "disease"), for it is upon this particular stone of stumbling that his internist fellow too often falls prostrate.

Mr. E. was sent to the clinic with his diagnosis correctly made by a colleague in a nearby city. He is, as you see, a man of thirty-nine, intelligent, ordinarily active, who aside from the disfigurement of his eruption, has evidently undergone a slump in general health, covering a period of two years, but most pronounced during the past fourteen months. He shows a pronounced pallor upon such parts of his face as are not involved in the cutaneous lesion. His hair is thinned, though not in a destructive way, his clothes hang rather baggily upon him, his whole appearance is that of a fatigue, a lassitude greater than his recent exertions would warrant. The eruption proclaims itself across the amphitheater—a florid, almost a livid dry redness of the entire face and forehead stopping below the ramus of the jaw at one or two points with almost pencilled sharpness.

There is no true edema. The lips are "chapped," and he moves his tongue and speaks as if his mouth were sore enough to make labial speech uncomfortable. The livid tinge extends down over the neck and onto the anterior chest, breaking up into islets which merge into a faint pink macular eruption involving much of the trunk. His hands present most interesting lesions—plaque-like infiltration of the finger-tips with the same bluish-red tinge as the eruption on the face, and here and there a distinct tendency to central depression that amounts almost to atrophy. On a close scrutiny of the face similar atrophy is apparent in spots over the cheek bones, and on the neck there are even a few that show the white atrophy that one learns to associate with the involuted lesions of erythematous lupus. The buccal mucous membranes and the lower lip show livid patches, confluent on the buccal and palatal mucosæ, among which one can again see, this time with a peculiar silvery tinge, the same suggestion of atrophic patching as on the skin. The tongue, while beefy red, does not show membrane, fissuring, or other breech of continuity. The patient's general examination reveals surprisingly little. His temperature is normal. His pulse is slightly accelerated, but of good quality. There is no cough, the chest is negative to physical examination and to the *x*-ray. The cervical lymph-nodes are very definitely enlarged, but there is no general adenopathy. The gaps at the site of a number of extracted teeth are apparent in examination of the mouth. Abdominal palpation reveals only a diffuse tenderness, no masses or doughy resistance, no fluid. The bones and joints are negative to inspection and palpation. There is no edema, and the cutaneous lesions of the hands are not reduplicated on the feet. A laryngoscopic examination (the patient is a trifle hoarse) is negative. But the urine examination discloses consistently the presence of hyaline casts and red blood-cells, and the blood-counts show red blood-corpuscles, 3,800,000; hemoglobin, 62 per cent.; leukocytes, 3400, with a differential count of 52 per cent. neutrophils, 45 per cent. lymphocytes, 2 per cent. large mononuclears, and 1 per cent. transitionals.

From the patient's history two facts stand out which sug-

gest that reiteration of this diagnostic discussion is not altogether trite. He has had two attacks of illness with fever in the past two years, the first diagnosed and treated as rheumatic fever, and the second as erysipelas. During this period he carried over the bridge of his nose and in front of his ears a sign-manual of his condition, in the form of patches of an eruption whose residue in atrophic scarring shows it to have been erythematous lupus of the discoid type. The chronic lesions are now lost in the flaming reddish purple of the acute eruption, but the whitish patching and the dry slightly scaling surface remain.

This patient presents then an eruption taken for erysipelas at one time, when it was accompanied by high fever and swollen lymph-nodes, and a history of joint manifestations and signs of chronic erythematous lupus at another. Erysipelas, erythema multiforme, and pellagra are the common misinterpretations of disseminate erythematous lupus in which the cutaneous symptoms are conspicuous. Malaria, rheumatic fever, tuberculous peritonitis, and when abdominal symptoms are uppermost, typhoid fever, or even gall-stones and chronic appendicitis are common sources of error.

Outstanding in this patient, then, is first, the dermatologic evidence of the generalization or extension of an erythematous lupus from the isolated chronic lesions on the face to an eruption covering the face, neck, and anterior thorax, and involving the fingers and hands. Make it an axiom, that when the eruption of chronic erythematous lupus begins to spread from the face to other parts, or to be associated with marked involvement of the mucous membrane, disseminated erythematous lupus impends. In the second place, hyperpyrexial attacks, of which this patient gives a good history, are characteristic incidents. In the third place, leukopenia, often of the most extreme grade, is highly characteristic, and even at the height of the fever, such counts as 3400 would not be unusual. I have seen counts as low as 1200 leukocytes in patients who recovered temporarily. The medley of symptoms which may accompany the picture is inevitably the source of diagnostic error. These symptoms are summarized as follows:

Systemic Symptoms of Disseminate Erythematous Lupus.—1. Attacks of high fever, running an intermittent (septic) course.

2. Joint pains, hydrarthroses, arthritis.

3. Subcutaneous abscesses, phlegmonous infiltrations, cellulitis.

4. Lymph-node enlargement, diffuse or localized, discrete or massive.

5. Abdominal symptoms, including especially pain in the upper quadrants, leading repeatedly to operation, often with negative findings.

6. Profound intoxication—delirium, apathy, torpor or toxic stupor.

7. Nephritis and nephrosis.

8. Symptoms of bronchopneumonia, often terminal.

The cutaneous lesions most often make the diagnosis—in fact, they are essential to a diagnosis. The patchy loss of hair which may almost suggest that of syphilis, and the deep flush of the face over the cheek bones with edema of the eyelids, though without outright erythematous lupus lesions, have not been mentioned. The latter, spoken of as "erythema facei perstans" was originally described as a separate entity by Kaposi. It should be remarked at this point that the macular eruption on the flanks is probably a toxic erythema due to salicin.

One of the most interesting objective comparisons of this clinical picture with others involves Libman's new type of vegetative endocarditis, in which cutaneous lesions appear not a little suggestive of those of disseminate erythematous lupus. In a case of the Libman type recently seen in my clinic, the paler, more granular, sharply localized patches of the eruption over the nose and cheeks, the lack of atrophy, and the generally more indolent character of the lesions on the hands, together with the physical signs of a pancarditis, made the differentiation easy.

The gravity of the prognosis in disseminate erythematous lupus must be its chief source of tragic interest for the practitioner. Attacking as it usually does young people between the ages of twenty-five and thirty-five, with a practically un-

broken record of fatal outcome within five years[1] and an obscure etiology, it is a formidable disease complex, still far from elucidation or control. Both streptococcal and tuberculous factors are urged as causative by individual proponents, the British speaking mainly for the streptococcal and the German and American literature for the tuberculous agent. It is certain that tuberculous mesenteric lymph-nodes, often overlooked at operation, appear too frequently at autopsy to be a purely coincidental finding. Yet much of the clinical picture strongly suggests a streptococcal element.

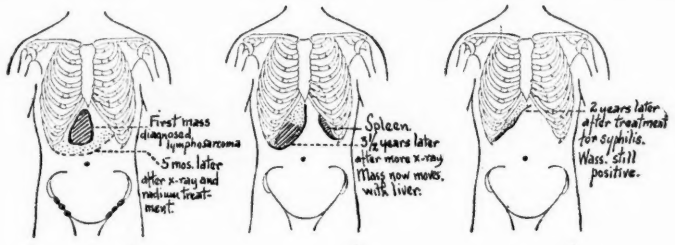
Treatment involves two factors. The first is quinin, which is tolerated by these patients in enormous doses (40 grains a day). The second is rest preferably in bed at first. The third is avoidance of intercurrent infection. The fourth is caution in attacking foci of infection except in periods of prolonged and complete remission. The extraction of infected teeth, or the removal of tonsils during an acute attack under the misconception that the process is "rheumatic," often results in a fatal explosion with almost unheard-of hyperpyrexia.

Case IV. The Problem of Malignancy in the Presence of Syphilis.—The patient before you, a colored man with a macroglossia, represents simply one phase of the problem of malignant change in its relation to the diagnosis and treatment of syphilis. This patient presents a marked thickening of the anterior half of the tongue, with a curious riddling of the tissue with stoma-like pustular openings. The entire process is of three months' duration and has, unfortunately for the patient, been accompanied by a persistently positive blood Wassermann reaction. I say unfortunately, not alone because it is a misfortune to have syphilis, but because it is particularly a misfortune to have it in coincidence with malignancy in the mouth and throat; for it is treated in far too many instances as syphilis and not as carcinoma, and the patient loses his life. This patient, while still living, was no exception to the rule. He was found to have a positive blood Wassermann reaction when he presented him-

[1] This patient has since died.

self with a lesion on the tongue, and *ipso facto*, it became syphilis in the opinion of his medical advisor. Six injections of neo-arsphenamin, given with this erroneous conception in mind, had produced little change in the lesion. On seeking further advice,

GUMMA OF THE LIVER, FIXED IN THE EPIGASTRIUM BY ADHESIONS, MAY BE MISTAKEN FOR A RETROPERITONEAL NEOPLASM



Male, aged eighteen, first examined in 1917.

Nodular Mass Right Upper Abdomen: Very tender, does not move with inspiration. Probable retroperitoneal lymphsarcoma. *x*-Ray chest negative.

No Blood Wassermann Test Taken. *x*-Ray Treatment Begun.

Five Months Later: Mass thought to be larger (in reality this was probably the liver edge). **Further *x*-Ray and Radium Treatment.**

Three Years Later: Mass as indicated at B. General health unchanged. Spleen recognized.

First Wassermann Test Taken: Strongly and repeatedly positive.

Diagnosis Revised: Mass now moves with respiration. Liver identified. "Syphilitic hepatitis with gumma."

Two Years Later After Treatment for Syphilis: Liver almost normal, spleen no longer palpable, general health excellent, blood Wassermann positive.

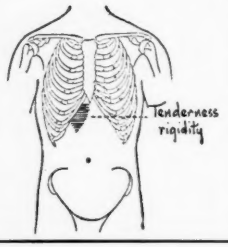
Youth, No History of Infection, Fixation of Mass and Lack of a Wassermann Led to This Diagnostic Error. Source of Infection Unknown.

FIG. 34.

a biopsy was taken and the nature of the lesion fortunately established. The result of the ensuing surgical intervention of course remains to be seen.

In what situations does the issue "Is this syphilis or is it malignancy?" assume the greatest diagnostic importance.

First of all, I should certainly place the lesions of the lip, mouth, tongue, and throat. Epithelioma of the lip is notoriously malignant, and the early lesions may strikingly simulate chancres. I have seen so perfect an imitation of a chancre on the right lower lip, accompanied by a positive blood Wassermann reaction and a pseudoroseola produced by examining the patient in a cold room (cutis marmorata), that I have insisted on a thera-



SIMULATION OF GALL-BLADDER MALIGNANCY AND CARCINOMA OF THE LIVER BY SYPHILIS. NO PREOPERATIVE WASSERMANN TEST TAKEN

Man, aged forty-two.

Examiner's Summary: "Tenderness marked in region of gall-bladder with slight rigidity. Gastric *x*-ray—three trials with belladonna—reports mass, extrinsic, stomach and duodenum negative."
Preliminary Diagnosis: Subacute cholecystitis.
Final Diagnosis: Probable malignancy of the gall passages, though possibly infected gall-bladder in anomalous position. Explore.

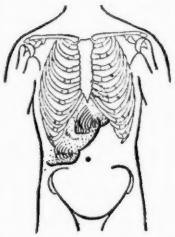
No Blood Wassermann Test Taken.
Operative Findings: "Liver filled with metastatic tumors, all sizes, having appearance of being malignant. Piece removed from one was found to be necrotic and did not show carcinoma, but clinically it is carcinoma. Gall-bladder contained no stones. Origin of carcinoma undetermined."
Pathologic Report: Necrotic Fibrous Inflammatory Tissue.
***x*-Ray Therapy was Ordered.**
Comment on History two years later, after 13 *x*-ray treatments with little change: "Inclined to question diagnosis."
First Blood Wassermann taken one month after above comment: Strong positive.
Palpable Mass and Enlargement of Liver with All Symptoms then Disappear under treatment for syphilis (6 arsphenamin injections).

Operative Appearances May Deceive. Take a Wassermann Before Exploring.

FIG. 35.

peutic test of three arsphenamin injections in six days to eliminate the possibility of a primary syphilis. Lesions of this type should not be subjected to manipulation and trauma for dark-field examination. If they bleed easily, they are probably carcinomas. The satellite bubo of the chancre is earlier to appear, larger, unilateral. In gumma of the tongue, malignant change is particularly apt to occur, is sometimes difficult to find until it becomes extensive, and may demand the excision of

an entire lesion or several parts of it for diagnosis while the patient is on the operating table, fully prepared for radical operation and radium implants, if frozen section reveals a malignant spot. It is much wiser to err in considering a lesion malignant and treating it as such, only to find later that it is "nothing but syphilis," than the reverse. It is equally important, however, never to lose sight of the syphilis, even though the lesion be malignant. I have seen preventable aneurysm follow



CARCINOMA OF THE LIVER IN SYPHILIS

Man, aged forty-nine.

This Patient, Apparently in Excellent Health and weighing over 200 pounds, complained of upper abdominal distress.
Physical Examination: Large hard rounded nodular liver containing definite masses on anterior surface. Pupils fixed to light. No jaundice or ascites.
Stomach Examination: Achlorhydria, 460 c.c. retention. *x*-Ray reported *negative*.
Blood Wassermann Reaction: Positive.
Neurologic Examination: Tabetic neurosyphilis with positive spinal fluid.

Diagnosis: Hepatic cirrhosis (?). Possibly non-specific hypertrophic cirrhosis.
Treatment: Two injections of arsphenamin intravenously, 0.2, 0.4 gm.
Result: Rapid development of ascites and edema of the legs. Death. Cause of death, clinical, nephrosis (?).
Autopsy: Massive *carcinomatosis of liver* from primary adenocarcinoma in pyloric ring. Pancreas, kidney, etc., negative.
Comment: Had it not been for the confirmatory neurosyphilis we might have thought this an example of false positive blood Wassermann in carcinoma. Apparently arsphenamin can cause a Herxheimer reaction in a carcinomatous liver, for no other explanation of the ascites and fatal outcome seems available. The excellent condition of the patient and the report of negative *x*-ray of the stomach led to premature dismissal of the diagnosis of carcinoma, although the retention should have suggested it. The achlorhydria occurs in both syphilis and carcinoma.

FIG. 36.

the ignoring of a syphilis accidentally discovered before excising an epithelioma of the lip, and have even had to deal with recurrent or rather new malignant degeneration of new gummas of the tongue on the half of that structure which remained following a hemiglossectomy in a patient whose coincidently discovered syphilis had been ignored after operation.

In the case of visceral malignant lesions in the presence of syphilis, the rule of giving precedence to operability has some

application. Syphilis of the stomach, for example, is a genuine rarity. Carcinoma of the stomach is relatively common. It is the height of folly, if the diagnosis remains in doubt after the Eusterman-Carman criteria have been applied to the case, to perform a therapeutic test for syphilis if the lesion is at all operable even though the patient have a coincident syphilis. In the case of the positively inoperable gastric lesion in the patient with syphilis, it is equally a mistake to dismiss the patient with a death warrant without treatment for syphilis. In both cases it is proper here to warn of false positive therapeutic tests, especially with the arsphenamins, which may give the mistaken impression of recovery while the carcinoma progresses. Failure to relieve pain in spite of weight gain and the continued presence of blood in the stools after the second week of treatment speak for carcinoma. Sudden hemorrhage must also be guarded against in the patient undergoing therapeutic test, and since neo-arsphenamin has a slightly greater tendency to produce vascular injury than arsphenamin proper, I prefer the latter or bismuth.

A somewhat different situation prevails in the case of the nodular liver, with jaundice and a suspected malignant origin. Here, if syphilis be present, exploration is mainly to satisfy the patient or to make a surgical diagnosis. If exploration be done, the surgeon should not, as in an instance I have known, be so convinced of the infallibility of his opinion that even the report of necrotic inflammatory tissue from frozen section is rejected, and the patient with a gummatous hepatitis sent for two years of *x*-ray treatment before even a blood Wassermann test is taken. In fact, in the diagnosis of abdominal surgical conditions, the preoperative blood Wassermann test is an absolute essential, and appearances on exploration no less than the physical signs before exploration may be totally deceptive. A therapeutic test deserves, in the main, precedence unless operation is insisted upon by the patient or required to eliminate other possibilities than malignancy. Here again, it must be remembered that the arsphenamins *should not be used*, either as operative preparation or as therapeutic testing agents, because of the disastrous effect of the therapeutic shock and the therapeutic paradox on pa-

tients who have the cirrhotic type of syphilis of the liver. I have, too, seen death within forty-eight hours follow the use of neo-arsphenamin in a patient with massive carcinomatosis of the liver who had coincidently a positive blood Wassermann reaction and asymptomatic neurosyphilis. The question as to false positive Wassermann reactions in patients with malignant disease involving the liver can, I think, be answered in the negative. In an examination of the records of 168 patients who had come to autopsy with carcinomatous livers, 2 had strong positive blood Wassermann reactions, 1 a weak positive, and 3 had incontestable syphilis. Both the patients with strong positive blood Wassermanns had syphilis. The weak positive blood Wassermann reaction was unsupported. Thus it appears that in any event the incidence of false positive blood Wassermann reactions in malignancy involving the liver does not exceed that normally to be expected as the margin of error of the average Wassermann technic.

CLINIC OF DR. RUSSELL S. BOLES

UNIVERSITY OF PENNSYLVANIA

EXTRAORDINARY DILATATION OF THE STOMACH SECONDARY TO MALIGNANT OBSTRUCTION OF THE PYLORUS. REMARKS ON THE EARLY DIAGNOSIS OF CANCER OF THE STOMACH

As the literature on carcinoma of the pylorus is so voluminous any attempt to discuss the subject in a general way at this time is unnecessary. In spite of the vast amount of study that has been expended on cancer of the stomach, the fact remains that comparatively few cases are diagnosed at a stage sufficiently early to offer any hope of permanent relief by either surgery or radiotherapy. At the Mayo Clinic, from October 1, 1897, to January 1, 1919, 2094 operations were performed for cancer of the stomach; of these, 746 were merely explorations, 612 were palliative operations, and 746 were resections, with a mortality of 13 per cent. In all, a formidable loss of life! With this situation in mind, it is my purpose merely to record a case, which, while similar to the majority of reported cases in many points, showed an extraordinary degree of dilatation of the stomach. I shall discuss a few points of special interest in connection with this finding.

CASE REPORT

J. M., an elderly man, a stage worker by occupation, was admitted to the service of Dr. Joseph Sailer, Philadelphia General Hospital, on October 31, 1925. His chief complaint was weakness of six weeks' duration, and loss of 15 pounds in weight during this period. He stated that until six weeks ago he had been perfectly well. Recently his appetite had been poor, and on one or two occasions he had vomited; no blood,

however, was noted in the vomitus. For the past six weeks he had been constipated; to his knowledge no blood had appeared in the stools. There had been some shortness of breath recently, and at times urinary frequency and inability to control urination.

Past History.—The patient had used alcohol until about six months before admission, and always drank before breakfast. He confessed to having had gonorrhea many years ago, and "a sore," which had never been treated, about twenty-five years ago.

Family History.—No information could be obtained concerning the patient's family history.

Physical Examination.—The patient was anemic, wasted, and appeared to be chronically ill. He weighed about 80 pounds, his best weight having been 120 pounds. Examination of the eyes showed the scleræ to be clear, the pupils irregular, equal, and reacting fairly well. The nasal septum was deflected to the right with resulting obstruction of the passage on the right side. The teeth were markedly carious. The mucous membranes were extremely pale, the pharynx and tonsils anemic, and the tongue coated. The chest was poorly formed and wasted. The lungs showed impaired resonance over the right upper lobe, harsh bronchovesicular breath sounds, and occasional râles at the right apex posteriorly.

The abdomen was soft, but distended. The liver extended just below the costal border. The spleen was not palpable. On inspection there could be observed a bulging of the abdominal wall about 3 inches in width, which extended from the upper left hypochondrium downward and across the abdomen to the right iliac fossa. This area was very prominent, and on percussion was tympanitic. Peristaltic waves of varying intensity surged over the area from above downward. This condition appeared to be caused by a distended stomach or colon, or both. No masses were palpable. Other physical findings were negative.

A tentative diagnosis of carcinoma of the stomach complicated with severe secondary anemia was made.

Gastric Analysis.—On several occasions gastric analysis was attempted, but each time vomiting occurred during the passage of the tube. The vomitus was semisolid and liquid, of sour odor,

and gave an acid reaction with litmus-paper. The bulk of the vomited material was greater than that of the test-meal, indicating retention. There was no free hydrochloric acid. The total acidity was 12; the test for lactic acid was strongly positive; the stomach contents were negative for free and occult blood; there were many Boas-Oppler bacilli.

Urinalysis.—A number of urinalyses were made during this patient's stay in the hospital and were negative for albumin, sugar, crystals, and urates. The specific gravity averaged about 1.010. A few leukocytes, an occasional epithelial cell, and some mucus were present.

Blood-count.—On November 1st, the red blood-cells numbered 1,580,000; white blood-cells, 8200; hemoglobin, 2.3 gms.; polymorphonuclears, 84 per cent.; lymphocytes, 14 per cent.; large mononuclears and transitionals, 2 per cent. The red cells showed a moderate change in size, but no change in shape. There was marked achromia.

The **Wassermann reaction** with the cholesterin antigen was 4 plus, with the Noguchi antigen 1 plus.

A **Roentgenologic examination,** made on November 10th, showed that there was retention of the entire barium meal. Fluoroscopic examination, with the patient in the prone position, pictured the entire abdomen occupied by the stomach, *which extended from the diaphragm to the middle of the pelvic cavity, and from one side of the body to the other.* There was a peculiar mottled appearance about the cardiac end and the greater curavature, and also at the pyloric end. This was thought to be due to the fact that the patient retained a large quantity of his food, probably for days at a time. The lesion was apparently an obstructing carcinoma of the pylorus (Fig. 37).

The patient was transferred to the service of Dr. Thomas for operation. At this time the lungs were fairly clear throughout. The heart tone was fair; there was a systolic murmur at the base and slight enlargement to the left. The patient was considered a poor risk for a general anesthetic.

Operation.—On December 3d, under ether anesthesia, the abdomen was opened by a midline incision. The stomach was

found greatly dilated and filling the entire abdomen. A hard, irregular mass occupied the pyloric end, causing the obstruction. No masses were felt in the liver, but the gall-bladder was enlarged and very hard. There were enlarged and indurated lymph-nodes about the stomach, and also small nodules throughout the

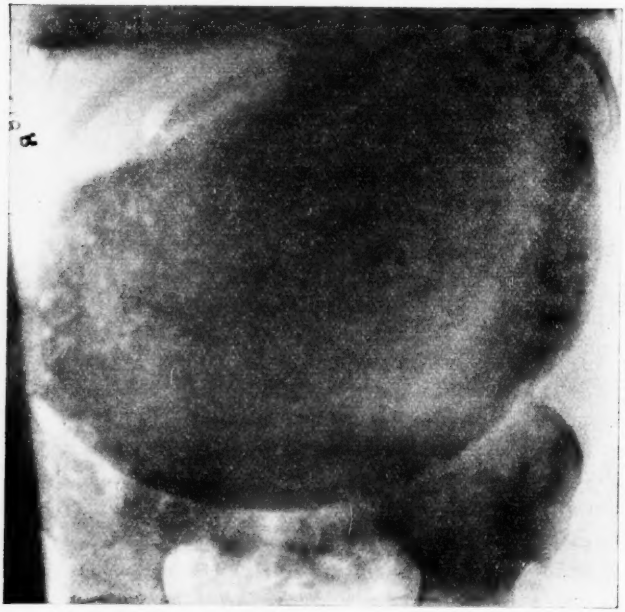


Fig. 37.—Roentgenogram showing extraordinary dilatation of the stomach, which occupies the entire abdominal cavity, extending from the diaphragm to the middle of the pelvic cavity, and from one side of the body to the other. Note mottled appearance at the cardia, along greater curvature and at the pyloric end.

mesentery. It must be borne in mind in connection with these nodes that such findings constitute merely presumptive and not conclusive evidence of metastasis. Involvement of the mesenteric glands of a benign nature may be associated with a malignant lesion, and yet be independent of it. The pancreas apparently was not involved. A posterior gastro-enterostomy was done.

The patient was in fairly good condition at the termination of the operation, but shortly after went into shock. He did not respond to treatment, and died at 9.30 P. M., six hours after the operation.

The final diagnosis was (1) carcinoma of the pylorus with secondary dilatation of the stomach, (2) metastasis to the gall-bladder.

Unfortunately, permission for an autopsy was not obtained.

DISCUSSION

The patient had a 4 plus Wassermann and a history of lues While time cannot be taken to discuss the interesting problems in differential diagnosis that this brings up, it may be remarked that syphilis of the stomach was not diagnosed for the following reasons: Syphilis of the stomach usually manifests itself as a diffuse sclerosis, a simple gastritis, or an ulcer. With the data at hand, it is reasonably obvious that none of these types of gastric pathology was present. There was no syphilitic lesion elsewhere and there was absolutely no benefit derived from antiluetic treatment. There was definite evidence of obstruction at the pylorus with complete retention, which is uncommon in syphilis. There was an increase rather than a diminution of the stomach capacity, and there was increased rather than decreased flexibility of the stomach wall as shown by the Roentgen rays. The rapid loss of weight and strength and early cachexia in this case render the diagnosis of lues improbable. Marked constitutional disturbance is infrequent as a result of syphilis of the stomach. Furthermore the coexistence of syphilis and carcinoma is too frequent to require comment.

While more or less dilatation of the stomach is a constant finding in all obstructive tumors of the pylorus, and is to be expected wherever there is any factor which diminishes the peristalsis and increases the resistant powers of the stomach, the enormous degree of dilatation encountered in this case is unusual. From a thorough search of the literature it would seem that comparatively few cases of this kind have been described. Falk,[1] in 1904, related the case of a woman, aged forty-eight,

who presented a distinct, smooth, and freely movable mass to the left of the uterus, which was thought to be an ovarian tumor. At operation a hard mass was found on the left side, at the junction of the inguinal and lumbar regions. This mass was firmly attached to the abdominal wall. A healthy ovary and uterus were found below and to the right of the growth. On closer inspection the mass was recognized as the stomach, which was displaced and so dilated as to fill the lower half of the abdomen. It had an opening in it at least 3 inches in diameter, through which the contents had escaped into the peritoneal cavity. The pylorus was the site of a carcinomatous growth as large as a goose egg. This condition accounted for the greatly dilated and displaced stomach, and the remarkable effort of nature to make an opening through the abdominal parietes. The patient died five days after operation of gangrene of the duodenum.

Another case of great dilatation of the stomach associated with carcinoma of the pylorus is related by Bosquier.[2] A woman, aged fifty, with icterus, complained of gastric symptoms and rapid emaciation. A diagnosis was made of gastric cancer with stenosis of the pylorus secondary to gall-stones. The patient was so extremely cachectic and emaciated that operation was considered dangerous. She succumbed in a short time—and autopsy revealed a greatly dilated stomach, extending entirely across the abdomen from left to right below the umbilicus. The liver was hypertrophied and contained numerous metastatic growths. The gall-bladder was the center of a metastatic mass and contained stones.

Recently Hunter[3] reported the case of a negro in whom he found an enormously dilated stomach, with complete stenosis of the pylorus. This was thought to be due to an old pyloric ulcer, but exploratory laparotomy revealed carcinoma.

The great problem in connection with gastric carcinoma is that of making an early diagnosis. On first thought we seem to be confronted with the discouraging prospect that of all our methods for making a diagnosis, be they physical, chemical, or roentgenologic, none offers unfailing data sufficiently early to insure a cure being effected in any given case. The usual text-

book symptoms, *i. e.*, indigestion, loss of weight, the presence of a tumor, evidence of pyloric obstruction, achlorhydria, etc., are almost valueless, inasmuch as they are all signs of an advanced process.

It has been shown that 33 per cent. of a large series of gastric cancer cases studied at the Mayo Clinic had no palpable tumor, and 46.7 per cent. had no food remnants to indicate obstruction. Cheever[4] analyzed 236 cases of gastric carcinoma treated at the Peter Bent Brigham Hospital, and in only 9.7 per cent. of these cases was it possible to attempt a radical operation. Yet the average duration of symptoms was less than six months. These figures are representative of the situation.

Roughly speaking, nearly 70 per cent. of cases of carcinoma of the stomach occur at or near the pylorus. Brinton[5] found that out of 360 cases of cancer of the stomach the pylorus was affected 219 times, or in exactly 60 per cent. of the cases. Carcinoma of the pylorus then constitutes the most important group of the gastric cancers. It is fortunately the easiest of recognition, and therefore stands a better chance of early surgical intervention. This is because a pyloric lesion produces the earliest symptoms and because Roentgen examination can reveal obstruction of the pylorus and dilatation of the stomach. Christian[6] calls attention to the fact that "at the earliest time there will be dilatation." Indeed, in some cases, it may be a question whether dilatation is secondary to carcinoma or vice versa, especially if we concede the fact that ulcer may be the precursor of cancer. Levin[7] and others insist that dilatation precedes ulcer, that dilatation involves irritation of the solar plexus, and this produces changes in the circulation and consecutive mechanical irritation of the pyloric mucosa. The local changes are complicated with spasms, infection of the mucosa, and adhesions. If we accept this line of argument, it is possible that carcinoma *may* be secondary to the conditions just described. In the author's case this seems unlikely, inasmuch as the patient never suffered from gastric symptoms until a few weeks before admission to the hospital.

The presence of symptoms for only six weeks in the case here reported would seem strange were it not for the fact that so

many cases of gastric cancer reach a hopeless stage without the manifestation of symptoms that arrest the patient's attention. It is quite inconceivable that the enormous dilatation found at operation could have developed within the brief period during which symptoms were in evidence. Since an unusual degree of dilatation is more commonly seen as a result of benign rather than malignant stenosis of the pylorus, in this case it is reasonable to suspect that an ulcer, which had later become malignant, was the primary cause of the stenosis. Einhorn,[8] in his text-book, makes the statement that perceptible dilatation of the stomach develops only in the course of time; and a little further on he says that all cases of cancerous stenosis of the pylorus reveal a more or less short period of illness (five months to one and a half years). He says the viscus is very much dilated in cases of cancer of the pylorus. The shape of the stomach may be distorted when the tumor descends by reason of its weight and drags the stomach downward into the pelvis.

There can be no question that the dilatation of the stomach in this case was absolute. Osler considers a stomach absolutely dilated when the capacity exceeds 1600 c.c. Some estimates place the average capacity of the unstretched stomach at 1500 c.c. The smallest normal stomach noted by Ewald could accommodate only 250 c.c. Ewald also observed a case of megalogastrica in which the stomach held 1680 c.c., and yet functioned normally. According to Carman,[9] an orthotonic adult stomach will accommodate 700 c.c. of a barium mixture without discomfort. Ordinarily, capacity increases as tone decreases, and pathologic variations of tone most frequently are the result of obstruction at the pylorus. Such obstruction is in most cases due to ulcer or carcinoma, although the extragastric tumors, pericholecystic adhesions, etc., must always be considered. Einhorn[8] states that abnormal size of a stomach is pathognomonic of pyloric stenosis only if the organ occupies nearly the entire abdomen and contains over 3 or 4 liters of fluid. The patient under discussion was frequently observed to fill with vomitus 2 large basins with a combined capacity of over 5000 c.c. (5 liters). In considering especially position, shape, and size, there

is no really standard or normal stomach from a roentgenologic point of view. Depending upon the habitus of the individual, all these properties are subject to wide variation, each being normal or appropriate to the owner. Mills in particular has made most interesting observations in this connection. Recognizing then that normal variations may have their limits, the Roentgen-ray standard roughly fixes the intercrestal line in the dorsal prone position, and 4 inches above that in the upright position, as the caudal limit of extension of the greater curvature of the normal stomach.

One of the unusual and interesting features of this case was the presence of visible and vigorous peristaltic waves running across practically the entire abdominal wall. Considering the degree of dilatation of this stomach, it was remarkable that any peristalsis could be detected, as only shallow and infrequent peristaltic activity is usually present in cancer. Barclay notes, however, that very powerful waves with periods of inactivity between indicate that peristalsis is wearing out. During the inactive periods in this case, peristalsis could be readily aroused by tapping the abdominal wall. Antiperistalsis, which is frequently observed in cases of pyloric stenosis due to cancer, was not present.

Since gastric carcinoma is an insidious disease, which may run an absolutely atypical course, with few symptoms and those often resembling functional gastric conditions, until the hope of radical cure is gone, we must be prepared for slight rather than marked alterations in the gastric picture. It is known that the changes may be so limited that no recognizable defect can be detected on *x*-ray examination, and yet the *x*-rays will reveal changes long before they are usually encountered clinically. At the Mayo Clinic, 95 per cent. of gastric cancers gave distinct roentgenologic signs of their presence. Indeed, in 1 case a carcinoma 2 cm. in diameter was detected. Of this 95 per cent. of cases, 50 per cent. were operable. An intelligent interpretation of the roentgenologic findings correlated with the facts gathered from the history, physical examination, and gastric analysis unquestionably enhances the hope of an early diagnosis. Carman[9]

states that the earliest time at which a cancer may be found depends upon:

1. The character of the cancer, whether a frank tumor, an insidious infiltration, or a cancerous ulcer.
2. Its situation.
3. The examiner's familiarity with the work.
4. The amount of roentgenologic evidence, together with the extent of clinical corroboration.

An early diagnosis should lead to early operation, and early operation should lead to a cure. Regarding operability in these cases it may be conservatively stated that a malignant tumor of the pyloric third of the stomach—the so-called operable zone—even if palpable, frequently lends itself to surgery with promise of a cure. Of course, palpability often means that the process is advanced and metastasis is presumably present. Should this be the case, or should ascites be present or perforation have occurred, a tumor in this location is then rendered inoperable.

It would seem that in the present state of our knowledge the only solution of the problem is in constant reiteration of the necessity of thorough examination in every case of persistent digestive disturbance in a person past the age of forty, and in the education of the public to the danger of neglecting what may appear to be trivial gastric symptoms.

When we encounter a fairly definite case of the disease we may well heed the statement made by Rehfuss,[10] who says, "My own experience teaches me more and more to regard gastric carcinoma as an acute lesion and to deal with it as summarily as is humanely possible."

BIBLIOGRAPHY

1. Falk, Charles C.: Carcinoma of the Pylorus, Internat. Jour. Surg., 17, 113, 1904.
2. Bosquier, R.: Cancer of the Pylorus with Icterus Due to Obstruction Simulating Gall-stone, Jour. de Sci. méd. de Lille, 37, 241, September 10, 1904.
3. Hunter, James W.: Roentgen Rays in the Negative Diagnosis of Cancer of the Stomach, Amer. Jour. Roentgenol., 14, 24, July, 1925.
4. Cheever, David: Personal Experience with Carcinoma of the Stomach, Boston Med. and Surg. Jour., 190, 401, March 6, 1924.

5. Brinton, W.: Quoted by Max Einhorn, Diseases of the Stomach, 1920, 6th ed., p. 299.
6. Christian, Henry A.: Cancer of the Stomach, Proc. Ass'n. American Physicians, 1924, p. 191.
7. Levin, G.: Connection Between Dilatation of the Stomach and Ulcer, Presse méd., Paris, 32, 577, July 9, 1924.
8. Einhorn, Max: Diseases of the Stomach, William Wood & Co., 1920, 6th ed., 299, 323.
9. Carman, R. D.: The Roentgen Diagnosis of Diseases of the Alimentary Canal, W. B. Saunders Co., 2d ed., 1920, p. 215.
10. Rehfuss, Martin: Gastric Carcinoma, Med. Clinics N. Amer., November, 1924, p. 729.

HODGKIN'S DISEASE—ABDOMINAL TYPE. REPORT OF A CASE WITH PRIMARY INVOLVEMENT OF THE RETROPERITONEAL GLANDS*

THE internal type of Hodgkin's disease, while perhaps not as rare as is commonly thought, is nevertheless, of unusual interest because of its relative infrequency and because of the many interesting problems encountered in its diagnosis. In this type the glands of either the thorax or the abdomen, or both, may be involved, the one group of glands usually being affected at an earlier date and to a greater extent than the other. The external glands in either case may be involved secondarily—enlargement of the cervical and axillary nodes supposedly following a primary thoracic process, and enlargement of the inguinal nodes being secondary to a primary abdominal process. This is exactly the reverse of the train of events that may occur in the ordinary external type of Hodgkin's disease, which is usually characterized by a progressive, painless enlargement of the cervical, axillary, and inguinal glands, with a later involvement of the mediastinal or abdominal glands. In both the external and the internal type there is ordinarily fever and anemia.

In the differential diagnosis of Hodgkin's disease the more common maladies to be considered are the infectious granulomata—tuberculosis and syphilis, the true neoplasms, which are usually sarcomatous in nature, and the leukemias. Although these diseases will not be discussed here, it may be mentioned that tuberculosis is one of the confusing conditions that most frequently enters into the differential diagnosis. Intensive investigation as to the part played by the tubercle bacillus in the causation of this disease began seriously with the studies of Sternberg in 1898. He contended that Hodgkin's disease was a form of tuberculosis, but later on, his own studies, and more

* Read before a meeting of the Philadelphia County Medical Society, January 13, 1926.

recently those of others—particularly the American investigators—have conclusively demonstrated that the tubercle bacillus is purely a secondary invader of the diseased structures, and in no sense a causative agent. In this rôle it is probably found no more frequently than many of the other organisms, which at one time or another have been suspected of being the cause of the disease.

The significant feature in the writer's case was the involvement, first, of only the retroperitoneal glands. Such an involvement as an initial symptom is exceedingly rare; when it occurs before other glands become affected, it may be referred to as "isolated glandular enlargement" or "localized Hodgkin's disease," which later becomes generalized. Williamson,[1] in recording a case of this type, lays emphasis on its rarity and the difficulty of diagnosis. In his case the diagnosis was not made until one of the inguinal glands became enlarged and was examined microscopically.

The interesting features in the case here reported are: (1) That the symptoms were mainly of the gastro-intestinal type and strongly suggested duodenal ulcer; (2) that enlargement of the axillary, cervical, and inguinal nodes did not appear until three months after operation for the primary retroperitoneal growth, at which time deep *x*-ray therapy was begun; (3) that, with the involvement of the external glands, the wrists became much swollen, and very tender and painful, and there was a rapid extension of this inflammatory process to the ankles and knees. This joint involvement, which was of significant interest in the case, suggests that the disease may be of an inflammatory and infectious nature. Furthermore, the case serves to emphasize the necessity of appreciating the fact that enlargement of the cervical lymph-nodes is not always the first manifestation of this affection. Symmers,[2] from a study of 15 cases of Hodgkin's disease, concludes that we must relinquish the conception that this disease is most commonly shown by enlargement of the cervical lymph-nodes. In his series the affection revealed itself frequently as an enlargement of the abdominal and thoracic lymph-nodes. He claims that the brunt of the attack is borne

by the nodes of the abdomen, thorax, neck, axilla, and groin, and by the auxiliary lymphoid systems in the spleen and liver.

It is interesting to note that the first case of the disease described by Hodgkin[3] appears to be an example of the internal form. The patient was a boy, aged nine years, whose abdomen was distended with ascites; the bronchial and abdominal glands were greatly enlarged and much indurated. Dreschfeldt,[4] in 1892, described 3 cases of acute Hodgkin's disease, in 2 of which there was no enlargement of the external glands. Since that time cases of the abdominal type have occasionally been reported; in these, the diagnosis was only made after external glands became involved, or at necropsy.

CASE REPORT

A clerk of Jewish extraction, aged forty-six years, married, when seen on September 2, 1924, stated that he had suffered from "indigestion" for years. For the past three months he had been subject to attacks of sharp, cutting pain across the upper abdomen and localized pain in the epigastrium. The attacks came on about three hours after eating, and were relieved by taking food. He had frequent nocturnal attacks which awakened him. The appetite was good. The bowels were constipated, the stools being of the spastic type; they were normal in color and contained no blood or mucus. Occasionally there was vomiting in the morning; the vomitus did not contain food or blood. During the past three months the patient had lost 18 pounds; this he attributed to the fact that he was afraid to eat. Except for the indigestion, he had always enjoyed good health. He used tobacco and alcohol moderately; he had never had any venereal disease. His mother died of "cancer of the uterus"; otherwise the family history was of no significance.

Physical examination revealed a fairly well-nourished man, who had some carious teeth, and diseased tonsils. The scleræ were clear; the pupils were equal and reacted to light and accommodation. The heart and lungs were negative. The upper part of the abdomen was distended, and there was very definitely palpable in the epigastrium a distinct nodular mass, firm and

slightly tender. The spleen did not appear to be enlarged; the liver extended about 1 inch below the costal border. There was no ascites. Possibly the right inguinal glands were slightly enlarged; no other glandular involvement could be detected. Proctoscopic examination was negative. The temperature was 98° F., the pulse 80, the blood-pressure 118 systolic and 74 diastolic. The weight was 148 pounds.

The urine was amber, flocculent, acid, with a specific gravity of 1.033 and a faint trace of albumin; there was no sugar and no acetone. The morning and evening specimens showed a large amount of indican. There were some hyaline casts, much mucus, some leukocytes, and occasional pus-cell, and a few epithelial cells.

The feces were yellow, apparently normal, with a faintly alkaline reaction. They contained a small amount of unchanged starch; the protein and fat digestion was apparently normal. There were no ova or parasites; no blood, free or occult, was found, and only a very little mucus which was well mixed. The bacteria were entirely Gram-negative, B. coli predominating, with a few B. mesentericus, a few long slender bacilli in chains, and an occasional spore.

The blood-count showed; red blood-cells, 4,210,000; leukocytes, 5200; hemoglobin, 75 per cent. Unfortunately, a differential count was not made at this time.

A fractional gastric analysis revealed nothing of significance.

The Wassermann reaction, on October 2, 1924, was negative.

Roentgenologic examination of the gastro-intestinal tract three months before the patient was first seen by the writer showed a defect of the duodenal cap, which was thought to be due to some outside pressure rather than to ulcer. A second roentgenologic examination of the gastro-intestinal tract, made by Dr. Ralph Bromer four months later, showed a slight enlargement of the right kidney. The twenty-four and forty-eight-hour examination revealed stasis in the transverse colon and moderate spasticity. With the patient in the prone position, the lesser curvature of the stomach appeared to be circular in outline. The roentgenologist thought this was caused by the

mass that could be felt clinically; he was certain that an enlarged right kidney could not cause this appearance, and believed that an enlarged liver afforded the most plausible explanation. The *x*-ray examination of the teeth showed no infection, but there was an unerupted left upper molar.

The preoperative diagnosis was retroperitoneal sarcoma.

The patient was operated upon on November 4, 1924, at the University of Pennsylvania Hospital, by Dr. George Müller. When the abdomen was opened through a left rectus incision a large retroperitoneal mass was seen, which extended from the lesser omental cavity to below the transverse mesocolon, and had pushed the stomach and liver forward, causing some obstruction at the duodenojejunal junction. This obstruction no doubt caused the initial gastro-intestinal symptoms which suggested duodenal ulcer. The presence of kinks and bands angulating and constricting the duodenojejunal juncture, and thereby producing a characteristic picture of peptic ulcer, has recently received considerable attention. There were many extensive glandular metastases in the peritoneum. One of these glands was removed for examination, the report on it being as follows: A frozen section of the lymphoid tissue shows it to be in a hyperplastic state. The capsule is slightly thickened, and shows no cellular invasion of its meshes by lymphoid tissue. The germinal centers are large and numerous. The lymphoid sinuses contain lymphocytes and endothelial cells.

Diagnosis: Hyperplasia of the lymphoid tissue.

Unfortunately this examination was confined to sections of frozen tissue only. The lymphoid hyperplasia, however, is usually the only histologic change noted at an early stage, not only in Hodgkin's disease, but also in streptococcic, tuberculous, actinomycotic, and other infections of the lymphatic apparatus. Again, excessive fibrosis may be the only finding in a gland which has been long affected by the disease. This may be so extensive as to destroy the characteristic histologic picture observed during the course of the disease.

On November 19th the patient returned for *x*-ray treatment, which was given in four courses by Dr. Pancoast and Dr. Pender-

Date.	Minutes.	Milli-amperes.	Kilivolts.	Filter.	Focal distance.	Portals.	Milliampere minutes.	Location.
FIRST COURSE: 1924 November 19th to December 2d.	75 each	4	200	Al. mm. 1 Cu. mm. 5	50 cm.	3	300 each	Abdomen anteriorly. Lumber region, right and left.
SECOND COURSE: 1925 January 5th to 14th.	75 each	4	200	Al. mm. 1 Cu. mm. 5	50 cm.	3	300 each	Abdomen, right and left, slightly oblique. Lumbar region posteriorly.
THIRD COURSE: 1925 March 2d and 3d.	11 each	5	130	Al. mm. 3 Glass mm. 1 Wood mm. $\frac{7}{8}$	24 cm.	5	55 each	Cervical region, right and left. Axillæ, right and left.
FOURTH COURSE: 1925 April 7th.	11 each	5	120	Al. mm. 3 Glass mm. 1 Wood mm. $\frac{7}{8}$	24 cm.	4	55 each	Cervical region, right and left. Axillæ, right and left.
April 9th.	50 each	4	200	Al. mm. 2 Cu. mm. 5	50 cm.	1	200 each	Abdomen anteriorly.

grass. These courses covered the periods from November 19 to December 2, 1924; from January 5 to January 14, 1925; and March 2 and 3 and April 7 and 9, 1925 (see table, page 318).

After the second course of treatment the original retroperitoneal mass was not palpable.

The patient returned on February 21, 1925, three months after operation, complaining that all his joints were aching; the wrists and ankles were swollen and tender. The first joints to be affected were the wrists, and the involvement then spread to the knees and ankles, which were stiff and painful. The patient stated that he had had a similar attack, though not so severe, earlier in the winter. Examination now revealed that the posterior cervical, axillary, and inguinal glands were all enlarged. They were freely movable, not tender, were not attached to the skin, and showed no evidence of breaking down. The patient stated that the left axillary glands had first begun to increase in size two days previously and the enlargement of the others followed rapidly. His weight at this time was 142 pounds (6 pounds less than on first examination). A cervical gland was removed for microscopic examination. The report of Dr. A. J. Bothe on this was as follows:

Gross examination: Specimen consists of a lymph-gland about the size of a small white bean. On section it is found to be well encapsulated, pinkish-white in color, and does not bulge.

Microscopic examination: Sections show loss of the lymph-gland architecture. The capsule is slightly thickened, and there is no evidence of cellular invasion. There is a fairly diffuse infiltration into the lymphoid tissue by columns of cells of two types; some of these appear as fibroblasts, while the majority are of the endothelial type. There are scattered throughout the entire section a number of giant-cells, which are fairly large, and contain from 2 to 4 centrally placed nuclei. The prevailing cell in the section is the mature lymphocyte. While there are no eosinophils present, the loss of architecture in this tissue, the presence of fibrosis, the proliferation of endothelial cells, and the presence of Dorothy Reed cells and polymorphonuclears suggests that we are dealing with a Hodgkin's type of pathology.

Diagnosis: Hodgkin's type of lymph-glands (Figs. 38, 39).

This report was confirmed by Dr. J. L. Goforth and Dr. Allen J. Smith.

Examination on April 2, 1925 showed that the glands of the left axilla, which at the former examination were more markedly enlarged than those of the right side, were still further increased

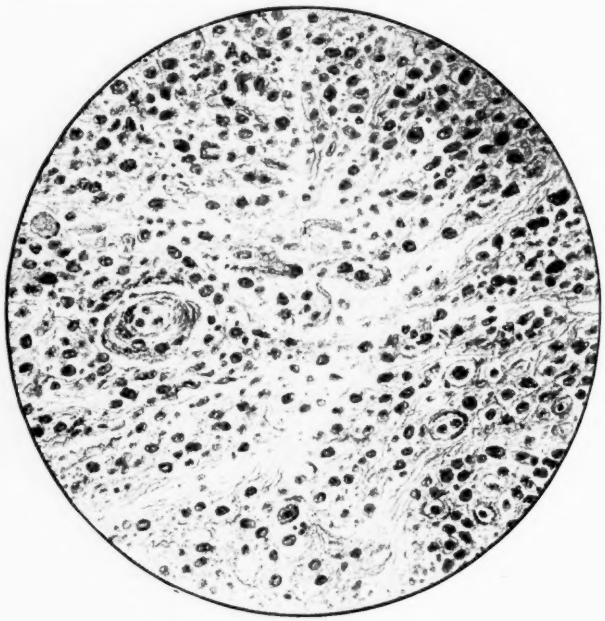


Fig. 38.—High power.

Section of lymph-gland showing: 1. Loss of architecture. 2. Diffuse fibrosis. 3. Proliferation of endothelial cells. 4. Presence of polymorphonuclear leukocytes. 5. Multinucleated giant-cells (Dorothy Reed cells).

in size, and the submaxillary, supraclavicular, and anterior cervical glands were involved. The glands above and below Poupart's ligament were much increased in size. The spleen was not palpable, there was no fluid in the abdomen, and the area of liver dulness was slightly enlarged. The joints of the hands, ankles, and knees were swollen and tender. During the months

of January, February, and March of this year (1925) the patient suffered every night from backache, chilliness, and fever. He stated that his joints first troubled him in May, 1924, when the hands and wrists became swollen and stiff. The acute condition of the joints, which suggested acute rheumatic fever, lasted from January 15th to March 15th. The patient's digestion was apparently normal, but easily deranged.

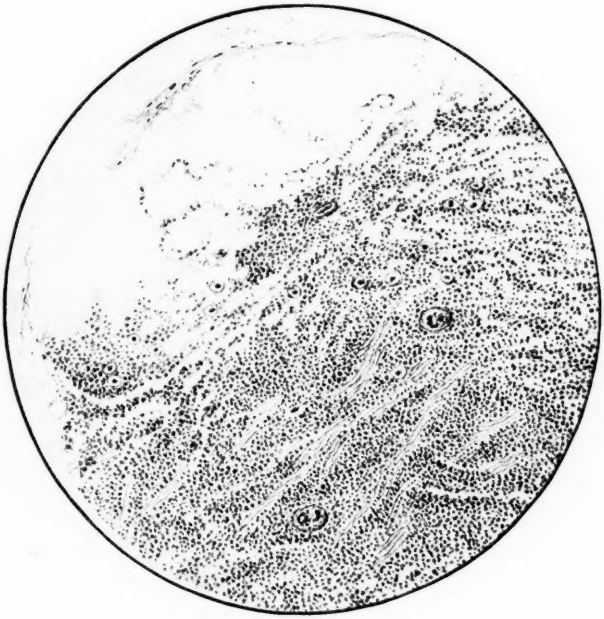


Fig. 39.—Low power.

On April 16th, two weeks later, the patient reported that he felt well, except for the stiffness still persisting in all the joints. He had lost 9 pounds and was growing weaker. The left foot and ankle were slightly swollen. Fowler's solution was prescribed at this time, but because of an idiosyncrasy he was unable to continue it. The cervical, axillary, and inguinal glands were still enlarged, though they had decreased somewhat in

size since the *x*-ray treatment. Whether or not this was the result of the treatment can only be surmised, as great variation in the size and consistency of any of the involved glands may occur during the natural course of the disease. The enlargement of the axillary glands was still somewhat greater on the left side than on the right. The inguinal glands were enlarged on both sides, but more so on the right. The spleen and liver were not palpable, but on percussion the lower border of the liver still extended two finger-breadths below the costal border. The upper border of the liver was normal. There was no ascites.

On May 15, 1925 the tonsils were removed by Dr. George Fetterolf. They were small, but very septic, and behind the posterior pillars there was found a mass of infected lymphoid tissue. Unfortunately no bacteriologic or histologic examination was made of the removed tonsils. This would have been interesting because of the strong suspicion that the throat and tonsils may serve as a portal of entry for infection, since the disease often starts in the cervical glands. There is substantial convincing evidence in the work of Bunting, Yates, Rosenow, Billings, and others, that this disease is produced by a specific organism, a diphtheroid bacillus and an ameba being the last to claim this distinction, and that consequently it is an infectious granuloma. Dr. Allen J. Smith, who has been examining sections of glands affected with Hodgkin's disease and supposed to contain these ameba, states that he has been unable to find them.

From June 5, 1925 to August 25, 1925 the patient received Coley's serum in increasing doses up to $5\frac{1}{2}$ minims. He refused injections beyond this point because of the reaction. During this interval the stiffness, pain, and swelling of the joints entirely disappeared, and, to use his own expression, he felt "completely rejuvenated."

On September 10, 1925 he reported that he had been suffering desperately from an itching, which began on the legs. Later it was localized to the abdomen, then the chest, and now to the head and neck. No structural change in the skin could be detected. Pruritus is a common manifestation of this disease, especially during its acute exacerbations. In this case a con-

siderable diminution of the eosinophil cells in the blood occurred, with a temporary spontaneous alleviation of the pruritus, a symptom which usually appears early and is difficult to control. For some weeks during the period of joint involvement a record of the temperature was kept. It varied from 96° to 101° F., and was of an irregular type, the afebrile periods being considerably longer than the febrile. Pyrexia is a fairly constant phenomenon in this disease, and may be irregular, intermittent, or relapsing in its course. It may represent the secondary infection of the lymph-nodes, which is frequently known to develop, or it may be the result of a specific toxemia.

The anemia, which is always associated with Hodgkin's disease, is one of its characteristic features. In this case the blood-counts were as follows: (The first three counts were made during the period of joint involvement.)

February 2, 1925: Red blood-cells 3,900,000; white blood-cells, 7500; hemoglobin 65 per cent.; polynuclears 53 per cent.; small lymphocytes 5 per cent.; large lymphocytes 25 per cent.; large mononuclears 1 per cent.; transitionals 8 per cent.; eosinophils 8 per cent.

March 3, 1925: Red blood-cells 4,450,000; white blood-cells 14,400; hemoglobin 67 per cent.

December 31, 1925: Red blood-cells 4,090,000; white blood-cells 9400; hemoglobin 74 per cent.; polynuclears 82 per cent.; large lymphocytes 11 per cent.; transitionals 2 per cent.; eosinophils 5 per cent. Blood-sugar 124.1 mg.; blood-urea 12.2 mg.; non-protein nitrogen 27.1 mg.; icterus index 10.

January 6, 1925: Red blood-cells 4,100,000; white blood-cells 8600; hemoglobin 78 per cent.; polynuclears 52 per cent.; small lymphocytes 4 per cent.; large lymphocytes 28 per cent., large mononuclears 2 per cent.; transitionals 4 per cent.; eosinophils 10 per cent.; blood-platelets 448,000.

These examinations presented the usual findings, namely, anemia of the secondary type, a slight absolute leukocytosis, and an increase of the eosinophil cells. Later there was a marked polynuclear leukocytosis, eosinophilia up to 16 per cent., and increase of the blood-platelets up to 448,000. Ordinarily the

leukocytes appear to increase with the course of the disease and an early lymphocytosis later gives way to a polymorphonuclear leukocytosis. Bunting has recently stated that a relative or absolute increase in the transitional cells and a total increase of the blood-platelets is a constant distinguishing feature of the disease.

On January 6, 1925 the patient stated that one week ago the left lower leg began to swell, the swelling gradually involving the entire leg, lower abdominal wall, and genitalia. After an *x*-ray treatment of the abdominal glands, this edema subsided and to date there has been no recurrence. This complication was undoubtedly due to pressure from enlarged retroperitoneal glands on the veins from the affected parts, and as soon as this pressure was relieved by the shrinking of the glands the swelling disappeared. Had it not been for the localization of the edema, it might have been thought to be of renal origin, as the urine at this time was observed to contain a heavy cloud of albumen, and hyaline and granular casts.

The blood-count (200 cells) at this time showed: Polynuclears 46 per cent.; small lymphocytes 5 per cent.; large lymphocytes 14 per cent.; large mononuclears 6 per cent.; transitionals 5 per cent.; eosinophils 16 per cent.; basophils 1 per cent.; red blood-cells 4,100,000; white blood-cells 8,600; hemoglobin 78 per cent.; blood-platelets 448,000.

January 13, 1925: Urinalysis showed a faint trace of albumen, and a few hyaline and granular casts.

January 30, 1926: Blood-count showed red blood-cells 3,940,000; white blood-cells 6050; hemoglobin 62 per cent.; polynuclears 84 per cent.; large lymphocytes 5 per cent.; large mononuclears 5 per cent.; transitionals 4 per cent.; eosinophils 2 per cent.

On April 3, 1926 the patient complained of some distress in the epigastrium after meals. He reported increasing weakness and constant drowsiness. The glands were all smaller, and with this reduction in the size of the glands there have occurred an amelioration of the pruritus and of the excessive heated feeling of the entire body, from which he had previously suffered. This sense of heat was now confined to the hands and feet.

Recently there had been some brownish pigmentation on the anterior surface of the left thigh. The heart action was very rapid, the pulse 128, and the temperature 102° F. The weight was 137 pounds. The patient had been complaining for several weeks of severe chills almost daily, especially when hungry or exhausted.

The criteria essential in making a diagnosis, which were established in this case, are as follows:

1. A primary enlargement of the retroperitoneal glands, followed by progressive painless enlargement of the posterior and anterior cervical, axillary, and inguinal glands. The glands were not tender. Individual nodes could be isolated and were freely movable. None of the glands was adherent to the skin, and none showed any evidence of breaking down. They varied from time to time in size and consistency.

2. Enlargement of the liver.

3. Progressive loss of weight and strength accompanied with fever that, in this case, was irregular in type.

4. The presence of secondary anemia with a polymorphonuclear leukocytosis, and an increase of the eosinophils and blood-platelets.

5. Pruritus.

6. Biopsy of glands, which revealed characteristic findings of Hodgkin's disease.

The literature seems to indicate that the case can have but one outcome. The only treatment that has proved of any value in Hodgkin's disease is roentgenotherapy, the success of which is usually most noticeable in the early cases, especially those in which the glands have not yet become fibrous. Some observers are convinced that the disease is curable in the early stages. Yates,[5] for instance, advises radical extirpation of all the tissue that can safely be taken from the affected region, followed by postoperative radiation of the site from which the tissue has been removed, preference being given to the *x*-rays. The radiation, however, should be carefully controlled by blood-counts in order to avoid a leukopenia. Successive radiations or excisions are carried out as indicated by the blood-picture and evidences of recrudescence. Symmers,[2] on the other hand, states that al-

though roentgenotherapy is often followed by a remarkable diminution in the size of the lymph-nodes, the outlook is hopeless. While it is true that life may be prolonged and distressing pressure symptoms may be relieved, the consensus of opinion is that no patient has ever been cured of Hodgkin's disease by radiation or by any other method.

On April 17, 1926 patient was admitted to the University Hospital to the service of Dr. Pendergrass. He was rapidly losing weight and strength and was retaining but little nourishment. He was troubled with a persistent cough and slept almost constantly. He developed a bronchopneumonia and died May 15, 1926, having been under observation continuously for over twenty months.

An autopsy was performed by Dr. McCutcheon of the University of Pennsylvania. Following is the report of the autopsy as submitted by Dr. McCutcheon and Dr. Baldwin Lucke. The fibrosis noted in the lymph-glands was probably partially induced by Roentgen-ray therapy.

Autopsy No. 11776–'26–468. Date, 5–15–1926 *University Hospital*
Services of Drs. Boles and Pendergrass. *Performed by* Dr. McCutcheon.
Name of Subject: B. M.
Admitted to Hospital: 4-27-1926.
Died: 5-15-1926.
Clinical Diagnosis: Hodgkin's disease.
Bacteriologic Diagnosis: No bacteriologic examination.

Gross Anatomic Diagnosis	Histologic Diagnosis
Hodgkin's disease.	
Heart: Normal.	
Spleen: Chronic hyperplasia and fibrosis.	Fibrosis: Hyaline degeneration of the arteries.
Liver: Hodgkin's disease.	Hodgkin's disease.
Kidneys: Normal.	Slight cloudy swelling.
Pancreas:	Normal.
Skin:	Superficial erosion.
Lymph-nodes: Right and left axillary. Peribronchial. Retroperitoneal.	Hodgkin's disease (fibrosing stage).
Lung: Bronchopneumonia. Tuberculosis, cavity formation, right apex.	Faulty resolution and partial organization.

REPORT BY DR. McCUTCHEON

External Examination.—Body of white, adult male, normal framework and moderately emaciated. Body is still warm. No edema, jaundice, or eruption. Scar of old laparotomy wound to the left of the umbilicus. Sclerae clear; no discharge from orifices. Genitalia and extremities negative. Hair distribution and skull normal.

Internal Examination.—Pericardial sac is normal. Pleural cavities free from adhesions.

Aorta.—Normal in caliber; no marked sclerotic changes.

Heart.—Weighs 250 gm.; normal in consistency. Epicardium smooth; myocardium normal in color. No changes in valves. Wall of left ventricle, 15; right, 5 mm. Aortic valve, 7; mitral, 9; tricupsid, 11; and pulmonary, 6 cm. No marked coronary sclerosis.

Abdomen.—Shows adhesions of omentum below the laparotomy scar. Peritoneum is smooth and glistening. Cavity contains about 50 c.c. of clear fluid. Diaphragm reaches to the fourth rib on the right side; fourth interspace on the left. Appendix free. Organs in normal position, except as described.

Spleen.—Weighs 220 gm.; tough. Capsule unthickened. On section pink, and fibrosed. Follicles not distinct.

Esophagus.—Grossly normal.

Stomach.—Moderate size, grossly normal. Gastric glands moderately enlarged along lesser curvature.

Intestines.—Are grossly normal. No lymphoid enlargement of mucosa.

Liver.—Weighs 2295 gm.; consistency increased slightly. Capsule unthickened on superior aspect of right lobe; on lower aspect of left are pale areas of new growth. On section some of these are quadrangular, some circular; these rather sharply demarcated and not encapsulated. Gross structure of liver tissue can be followed for some distance into these areas and in this respect they do not resemble tumors; largest of these areas about 4 cm. in diameter. Many other smaller, more infiltrating areas of new growth, are found, especially in the right lobe, otherwise the liver tissue presents the usual appearance in regard to color and markings.

Gall-Bladder.—Is grossly normal. Bile is readily expressed into duodenum.

Pancreas.—Consistency increased; lobulation normal. Neighboring lymph-nodes are somewhat enlarged, scarred, and do not encroach on pancreas. Mediastinal and peribronchial lymph-nodes are not enlarged.

Adrenals.—Grossly normal. The left embedded in a mass of scarred lymph-nodes.

Left Kidney.—Weighs 175 gm.; right, 130 gm. Capsule strips easily, leaving a smooth surface. On section normal color; cortical striations somewhat less distinct than normal. Corticomedullary junction distinct.

Left ureter is embedded in scar tissue as it crosses the iliac artery, but no hydronephrosis is present.

Urinary Bladder.—Is grossly normal.

Prostate.—Slightly enlarged. The mesenteric lymph-nodes show little change. Lymph-nodes along the aorta are intensely scarred, pale pink, and embedded in a mass of dense white scar tissue; the same is true of nodes along the left iliac artery. Axillary nodes are normal in size and indurated. Inguinals and cervicals not palpable.

Sections from the lung, peribronchial lymph-node, right and left axillary lymph-nodes; retroperitoneal lymph-nodes; spleen; liver, and kidney.

Sections were prepared and examined histologically from the following parts: (1) Lung, (2) liver, (3) spleen, (4) kidney, (5) pancreas, (6) skin, (7) lymph-nodes.

Lung.—The pleura is moderately thickened, fibrosed, and covered with a layer of low cuboidal mesothelial cells. The architecture of the lung is considerably distorted. In most areas the air spaces are either collapsed or else filled with hyalinized fibrin exudate in which lie occasional leukocytes and young connective-tissue cells. The alveolar walls are somewhat thickened and many are adherent to one another. Many of the capillaries are completely collapsed; others, however, are considerably engorged. Several large bronchi are packed with pus cells; their mucosa is partly lost and they usually have edematous

walls infiltrated with leukocytes. In a few areas the lung tissue approaches the normal, but here the air spaces are flooded with erythrocytes and many contain phagocytic cells laden with carbon pigment. The arteries have a somewhat irregularly thickened and partly hyalinized intima; the internal elastica is split and much proliferated.

Liver.—In many areas there are masses of peculiar granulation tissue, consisting of densely interwoven delicate fibrous strands in which lie great numbers of large multinucleated giant-cells (Dorothy Reed cells); the nuclei of these cells take a deep purple stain. Here and there are scattered a few eosinophils, but they are nowhere conspicuous. Many of the fibrocellular masses occupy several low-power microscopic fields. Elsewhere in the liver smaller areas of like composition are encountered, occurring particularly at the lobular peripheries. The liver tissue proper is not separated from the new growth and in many places tongues of liver tissue extend into the granuloma. The hepatic cells have the usual arrangement, but they are generally swollen, poorly outlined, and many have lost their nuclei.

Spleen.—The capsule is moderately thickened, its outer portions are very edematous and infiltrated with small round cells, eosinophils, plasma-cells, and larger endothelial elements. Trabeculæ are of average size. The splenic structure is preserved, but there is an evident overgrowth of the stroma and the walls of the blood-channels are distinctly prominent. The sinuses contain, chiefly, erythrocytes, with occasional intermingled larger mononuclear elements; they are lined by prominent endothelial cells. The splenic pulp is scanty, and in addition to the usual cellular elements there are seen occasional large multinucleated giant-cells. The central arteries have thick hyaline intimal coats. The Malpighian follicles are small, densely packed, and in many are seen small irregular hyaline masses. No granulomas, such as occur in the liver, are encountered.

Kidney.—Capsule is normal. The stroma shows no proliferative changes. The general architecture is normal. The capillaries, in both cortex and medulla, are inconspicuous. Glomeruli are of average size, normally nuclear, and have poorly

filled coils; the capsule of Bowman and its lining cells are normal. The convoluted tubules are lined by moderately swollen poorly preserved cells which are frequently devoid of nucleus; many of the cells contain small vacuoles. Similar changes are seen in the limbs of Henle. The collecting tubules are normal. A few larger branches of the renal arteries have a slightly irregularly thickened intima.

Pancreas.—The stroma is normal. The lobules are of average size. Acini are normal. Islands of Langhans are numerous and consist of well preserved, normally appearing cells.

Skin.—The epiderm is normal. The corium is slightly edematous, and free from cellular invasion. A number of sweat glands are normal. At one area there is a superficial erosion; here the epiderm is absent, its place being taken by a hyaline necrotic mass in which are embedded a number of dark pyknotic nuclei. Processes of newly-formed regenerating epiderm are seen to extend into and beneath the scab.

Lymph-nodes.—Sections are taken from the right axillary, left axillary, peribronchial, and retroperitoneal lymph-nodes. The changes are similar, but most marked in the axillary nodes, which have a thickened, fibrous capsule. The interior of the node shows much disorganization. Many vessels are surrounded by extremely thick hyaline mantles, and in addition there are many places of roundish hyaline bodies having no discoverable relation to the vascular supply. The sinusoids contain eosinophils, as well as large proliferated reticular cells. The stroma is prominent. The lymphoid tissue has been partly replaced by epitheloid cells, as well as by hyalinized fibrous scars.

BIBLIOGRAPHY

1. Williamson, C. S.: Hodgkin's Disease, Abdominal Type. Med. Clinics North America, 7, 387, September, 1923.
2. Symmers, Douglas: The Clinical Significance of the Pathologic changes in Hodgkin's Disease. Amer. Jour. Med. Sci., 167, 313, March, 1924.
3. Hodgkin, quoted by Sir Samuel Wilks: Guy's Hospital Reports, 11, 57, 1865.
4. Dreschfeldt: Acute Hodgkin's Disease. Brit. Med. Jour., 1, 893, 1892.
5. Yates, J. L.: An Outline of Twelve Years' Study of Hodgkin's Disease and Allied Affections. Wisconsin Med. Jour., 19, 447, 1920–21.

CLINIC OF DR. WILLIAM D. STROUD

PENNSYLVANIA HOSPITAL

THE VALUE OF QUINIDIN SULPHATE IN THE TREATMENT OF AURICULAR FIBRILLATION

THIS article is a preliminary report of our results in the treatment of 134 patients with auricular fibrillation observed on the wards (of Dr. George W. Norris' Service) and in the Heart Clinic of the Pennsylvania Hospital; in the Heart Section of the United States Veterans' Bureau, District No 3, Philadelphia, and in the private practice of the author. These observations were made between March 1, 1921 and March 1, 1926. They are inspired in part by the numerous reports of the results in the treatment of this arhythmia which have appeared in various parts of the world during the past five years, but mainly by the observations of Levine and Wilmaers.[1] As stated in their summary, it is suggested that quinidin sulphate is of no practical value in the treatment of patients with auricular fibrillation who previously have had congestive heart failure, and that the more conservative treatment with digitalis is the more satisfactory. They also conclude that the use of quinidin should not become general, but should be confined to a few who might still be making careful observations as to its proper place in the treatment of heart disorders. Since in our treatment with quinidin sulphate of 42 of the 134 patients with auricular fibrillation we have had no deaths which, in our opinion, can be in any way attributable to the toxic effects of this drug, and as in only 2 patients were there even suggestively serious toxic symptoms, and as there apparently have been no ill effects at all in the treatment of many ambulatory cases with multiple premature contractures and paroxysmal tachycardia, we are loathe to assent to the restric-

tion to the extent suggested by these authors in the use of what has seemed to us a valuable drug.

In 1922 Reid,[2] in reporting on a case of respiratory paralysis following quinidin therapy, states that "Apparently the occurrence of paralysis of respiration is rare." Von Frey,[3] who introduced quinidin in cardiac therapy, has reported 2 cases in his second report,[3] and, more recently, a third was described by him and Hagemann.[4] One of Haass'[5] patients, who had taken 2.8 gm. (43 grains) of quinidin in three and a half days, suddenly became pulseless and cyanotic, and stopped breathing, after which a regular rhythm set in. In this case it is probable, as Wilson and Hermann[6] suggest, that the difficulty was due to the Stokes-Adams syndrome in heart-block, the cessation of respiration following rather than preceding heart-block. Cohn and Levy[7] say that 4 cases are reported in the literature, in all of which recovery occurred.

Lewis,[8] in his discussion of quinidin therapy in 1922, referring to respiratory paralysis, writes: "Whether this method of small trial doses will eliminate danger from this source remains for the future to decide." Reid[2] found no clue as to patient's idiosyncrasy to quinidin in his test doses on the patient on which he reports. He concludes: "Paralysis of respiration following quinidin therapy is a rare occurrence." Our observations most certainly add emphasis to this conclusion.

Burwell and Dieuaide,[9] in their series of 16 cases of auricular fibrillation treated with quinidin sulphate, claim that they were able to give this drug "until the cardiac mechanism became normal, or until unfavorable signs appeared, or until it became evident that the rhythm could not be changed. In 1 case 19 gm. of the drug was given. No untoward effects except headache and an increase in the number of stools were observed." They conclude: "Two grams of quinidin sulphate may be administered daily without the production of severe toxic symptoms." Also, that "so far as is known at present, the danger associated with the use of this drug lies not in its direct effects, but in embolism from an intra-auricular thrombosis following the onset of normal auricular activity." We believe and feel that it should be

generally accepted as a fact that embolism occurs as commonly in cases with auricular fibrillation not treated with quinidin sulphate as in those either successfully or unsuccessfully treated with this drug.

In 1923 Korns,[10] in an excellent article on this subject, writes: "A review of the literature establishes the fact that in any given case of auricular fibrillation one can never predict whether or not quinidin will be able to restore a normal mechanism, or, once restored, to maintain it. With this fact my own clinical experience with quinidin is in complete agreement. Incidental circumstances, such as the character of the cardiac lesion, the degree of decompensation, the duration of the disordered mechanism, the age of the patient, etc., are not essentially related to failure or success with quinidin." Our experience during the past five years at the Pennsylvania Hospital is almost an identical one. Korns[10] further states: "In order to gain a comprehensive conception of the contribution of auricular fibrillation to heart failure it is essential that a normal cardiac mechanism be secured in as many cases as possible. Before proceeding further we must inquire into the nature of the drug's direct effect, and we find that quinidin is a muscle poison which exerts a distinctly depressant action on the myocardium. Whereas digitalis enjoys almost universal application in cardiac failure, the use of quinidin must be restricted not only to those cases of decompensation (cardiovascular failure) which have auricular fibrillation, but still further within that group. In every case we must decide as nearly as possible whether the benefit to be expected from resumption of normal rhythm will outweigh the harmful effect of quinidin as a muscle poison."

We have quoted at considerable length the opinions of others as to the toxicity and dangers entailed in the use of quinidin sulphate in patients with auricular fibrillation. Our object is to show that, while fully realizing that this drug must be used with caution, yet, after careful observation in 134 cases, we believe its use in 42 patients has been justified, and in 27 of these most satisfactory results have been obtained. Although quinidin sulphate is contraindicated in congestive cardiovascular failure—

except in a few unusual cases—still, in the majority of cases with auricular fibrillation, after a return to the greatest possible efficiency of the circulation with rest, diet, and digitalis has been obtained, quinidin sulphate should be used in an attempt to obtain a return of sinus rhythm and thus materially further the improvement of the circulation.

The question as to how much the arhythmia makes worse an already impaired circulation seems to have been finally answered by Bloomguard and Weiss,[11] reporting on their work at the 1926 meeting of the American Association of Physicians at Atlantic City. By injecting certain emanations of radium C in the vein of the right arm and with a radium detector determining the time of arrival of these emanations in the artery of the left arm, they have at last found an apparently perfect method of determining the rate of blood flow in individuals with normal and abnormal cardiovascular systems. This rate of circulatory flow in the normal individuals appears to be between fifteen and twenty-two seconds, *i. e.*, from the vein of the right arm, through the right heart, lungs, and left heart to the arteries of the left arm. In auricular fibrillation there is a retardation of the circulatory flow which varies directly with the clinical condition of the patient, it being well over twice the normal in certain cases of auricular fibrillation with congestive heart failure. They believe this retardation is due to three factors: (*a*) the arhythmia, (*b*) the myocardium, and (*c*) valve lesions; and that the exact amount of circulatory retardation attributable to each of these three factors varies with each patient. Variations in vital capacity do not correspond with retardation of circulatory flow, and this possibly in part explains what seems to us a false impression which Levine and Wilmaers[1] received, namely that on a return to normal sinus rhythm with quinidin sulphate no benefit accrued to the patient since the vital capacity was not improved. In other words, from Bloomguard's and Weiss' work, it would seem that a patient with auricular fibrillation can be given a more efficient circulation by successful treatment with quinidin sulphate and yet there be no demonstrable improvement in the vital capacity. In 4 patients with auricular fibrillation, well

controlled by digitalis therapy, when a rhythm of sinus origin was obtained with quinidin sulphate, the retardation of circulatory flow from the vein of the right arm to the arteries of the left was decreased from thirty to twenty-five seconds; twenty-eight to twenty-six seconds; forty-four to twenty-eight seconds, and thirty-eight to twenty-five seconds, respectively. These findings it would seem to us are the most conclusive as yet brought forward to prove the advisability of attempting with quinidin sulphate to restore a normal sinus rhythm in all patients with auricular fibrillation in which this seems practical and proves possible.

We realize that many individuals with auricular fibrillation who have had congestive heart failure in the past are leading happy, useful lives with their auricular fibrillation well controlled with digitalis. There are several such cases among our series, namely:

Case I.—Miss R. H., aged fifty-eight. White, no occupation.

History, Present Illness.—At the age of seventeen she was told that her heart was not quite normal and was given tincture of digitalis. When twenty-five years old had a severe attack of acute rheumatic fever. Until 1915 the patient continued to take small doses of tincture of digitalis; during this year the rhythm of her heart suddenly became irregular and she was first seen by Dr. Joseph Sailer who made the diagnosis of auricular fibrillation. She was placed upon a treatment of restricted effort, diet, and pulverized digitalis, gr. $\frac{1}{2}$, t. i. d. The author first saw this patient on April 5, 1924. At that time she had been confined to bed for three weeks with mild breathlessness and cardiac palpitation. For the past five years she had been forbidden by another physician to mount any flights of stairs and had not been allowed to attend the theater, and, in fact, had almost been confined to her room. Dr. Sailer had not seen her since 1915. The author's first examination revealed a definite systolic heave to the precordium, with the apex-beat in the sixth interspace, and an easily palpable systolic and at times a diastolic thrill. The rhythm was definitely that of auricular fibrillation with an apical

rate of 104 and a pulse rate of 68. A harsh systolic murmur could be heard at the apex with a long rumbling diastolic murmur, most noticeable during the longer diastoles. The blood-pressure was systolic 188, diastolic 84. The patient was taking pulverized digitalis, ½ grain, twice a day. This dose was increased to ½ grain t. i. d. On April 8th the patient was much more comfortable with practically no breathlessness and no palpitation. The apical rate was 80 and the pulse rate 70. The patient was allowed out of bed, and since that time has not been confined to bed because of cardiovascular symptoms for a single day.

On January 6, 1925 the apical rate was 88 and the pulse rate 72. Blood-pressure was systolic 170, diastolic 74. For the past month the patient had felt somewhat more breathless on effort than previously. She had been going up 15 to 20 steps twice a day and attending the theater at least once a week. The digitalis was increased to 1 grain twice a day, with satisfactory results.

On February 24, 1926 the patient felt comparatively well and had been continually increasing her activities. Heart rate 66, pulse rate 66; blood-pressure was systolic 168, diastolic 68. She was still taking pulverized digitalis 2 grains a day.

Case II.—Mr. B. G., aged fifty-two. Italian. Stone carver from the age of eighteen.

History, Present Illness.—Patient was treated in the wards of the Pennsylvania Hospital with acute rheumatic fever in 1901. (He was then twenty-one years old.) Again, in 1913 and in 1915, he was confined to bed with severe attacks of acute rheumatic fever. He first came to the Pennsylvania Hospital Heart Clinic complaining of breathlessness and palpitation while at work on April 13, 1921.

Physical examination on the above date revealed an ambulatory patient with slight breathlessness at rest. Respiratory rate 26 per minute. Height 5 feet, 8¼ inches; weight 153 pounds. Blood-pressure: systolic, 185; diastolic, 110. The tonsils were buried and cryptic and the teeth were evidently a

focus of infection. There were rapid, visible irregular pulsations in the neck and there was a definite, diffuse systolic heave to the precordium. The apex-beat was palpable in the sixth interspace, but no definite thrills were felt.

L. B. = 14 cm. in the sixth interspace.

R. B. = 3.5 cm. in the fourth interspace.

P. M. D. = 5.5 cm. in the first interspace.

The ryhthm was typically that of auricular fibrillation with a systolic murmur at the apex and also a diastolic in this area. The apical rate, 144; pulse rate, 108.

Since this date the patient has taken between 20 and 30 drops of tincture of digitalis t. i. d., and has not missed a day at work because of cardiovascular symptoms. He has continued to attend the Heart Clinic every two weeks for the past five years. His last visit on March 18, 1926 found him weighing 158 pounds with an apical rate of 96 and a pulse rate of 96, and a blood-pressure: systolic, 178; diastolic, 100; vital capacity, 3650.

L. B. = 14.5 cm. in the sixth interspace.

R. B. = 3.5 cm. in the fourth interspace.

There was no evidence of any congestive cardiovascular failure.

Laboratory Findings.—April 18, 1921: Blood Wassermann negative; urine at no time has shown albumen, blood-cells, or casts. The blood chemistry has always been within the normal limits.

Electrocardiographic Findings.—April 18, 1921: (1) Auricular fibrillation.

(2) Left ventricular preponderance.

(3) Diphasic T-waves in all three leads.

September 30, 1924: (1) As above.

(2) As above.

(3) T-waves upright in all three leads (this in spite of the 30 drops of tincture of digitalis t. i. d.).

We have several cases which have been under our observation for a full five years with auricular fibrillation and slow ventricular rates, seemingly as comfortable and able to maintain

as efficient a circulation without digitalis as with this drug. We will briefly describe 2 such cases.

Case III.—Mr. L. S., aged sixty-seven. Italian. No occupation while under our observation.

History, Present Illness.—Patient was comparatively well prior to his admission to the Pennsylvania Hospital on April 16, 1920, with an attack of congestive heart failure accompanied by auricular fibrillation.

In the past the only history of illness that could be obtained was of acute rheumatic fever when a boy of sixteen or seventeen years in Italy.

This patient has been seen in the Pennsylvania Hospital Heart Clinic practically once a month since 1921. Since that time he has shown no evidences of congestive heart failure. His apical rate has varied between 104 and 64 and his pulse rate between 70 and 64. Blood-pressure: systolic, between 142 and 120; diastolic, between 85 and 70. His vital capacity has ranged between 2400 and 2750.

L. B. = 16 cm. in the fifth interspace.

R. B. = 4 cm. in the fifth interspace.

Treatment.—At times he has taken between 15 and 20 drops of tincture of digitalis three times a day, but the majority of the time he has taken absolutely no medication. At times during these six years he has gone for ten to fifteen weeks with no tincture of digitalis. Of course, he has done no work and has led an absolutely sedentary life, but this life has been a happy one, and for the past five years he has not been totally incapacitated because of his heart for a single day.

Electrocardiographic Findings.—December 14, 1925: (1) Auricular fibrillation.

(2) Left ventricular preponderance.

Case IV.—Mrs. J. C., aged ninety-two. White housewife.

History, Present Illness.—Was first seen by the author in January, 1922 because of a mild upper respiratory infection. She complained of a slight cough for the past few days and a

sore throat. No precordial pain. Had been somewhat short of breath on effort since the age of eighty-six (1916). At that time a physician had told her that her heart was markedly irregular; but she had taken no medication since then except for an occasional laxative and had not seen a physician during the past six years.

Physical examination revealed a well-preserved, cheerful, old lady with a temperature of 99⅘° F., respiration of 24. Blood-pressure: systolic, 168; diastolic, 92. Apical rate, 98; pulse rate, 88. The apex-beat was in the fifth interspace and there was a slight systolic heave to the precordium with the more forceful systoles. No thrills were felt.

L. B. = 13 cm. in the fifth interspace.

R. B. = 4 cm. in the fourth interspace.

The rhythm was typically that of auricular fibrillation, but no murmurs were heard. No evidence of congestive cardiovascular failure were demonstrable.

Shortly after this the patient moved from Philadelphia to a town in Ohio, but a letter was received from the daughter in June, 1925 saying that her mother was apparently well and happy at the age of ninety-five, and had not seen a physician or taken any medicine since the author's visit three years before.

Finally, we should like to report upon 5 of our 27 cases of auricular fibrillation with previous congestive cardiac failure successfully treated with quinidin sulphate, in which we feel that the results with this drug have been most strikingly satisfactory.

Case V.—Mr. H. H., aged sixty-one. White sales engineer.

This patient was referred to the author on September 29, 1924 by Dr. Richard W. Finley, of Cleveland, Ohio.

History, Present Illness.—Patient was comparatively well until May 1922 except for slight breathlessness on effort. At this time he began to be quite breathless and noticed that his heart beat very irregularly. There was no definite edema of the lower extremities, but much gastric distress and pain over the region of the liver. Except for an attack of acute rheumatic

fever at the age of sixteen years, and recently numerous "abscessed teeth," he gave a negative past medical history.

He had been married for twenty-six years, but his wife had only one pregnancy, which was extra-uterine. Otherwise the family history was not relevant.

From the onset of his symptoms, in May, 1922, the patient was put to bed and given 30 minims of digitalis a day. He gradually grew worse, with increasing breathlessness, abdominal distress, and definite ascites, until June, 1924, when he was sent to Dr. Finley, whose findings were as follows: "Chronic valvular endocarditis, mitral stenosis and insufficiency, with a preponderating enlargement of the right ventricle and the right auricle, extending 5 to 6 cm. to the right of the sternum. The apex of the left ventricle was in the left fifth interspace. The liver was palpable and tender and he was having great trouble with digestion. There was no edema of the lower extremities. His pulse showed a characteristic auricular fibrillation and electrocardiograms showed the same thing. I put him on quinidin sulphate, and by the time he had taken 65 grains he had a normal mechanism. He has taken 5 grains a day since and has improved remarkably in his endurance and capacity for exercise."

On October 15, 1924 his weight was $118\frac{1}{4}$ pounds; blood-pressure: systolic, 142; diastolic, 80; apical rate, 100; pulse rate, 100. The apex-beat was palpable in the sixth interspace and there was a marked systolic heave to the entire precordium and the lower end of the sternum.

L. B. = 12 cm. in the sixth interspace.

R. B. = 3 cm. in the fourth interspace.

The first sound at the apex was definitely snappy in quality and accompanied by a harsh systolic murmur. When recumbent on the left side a long, harsh diastolic murmur could also be heard. The rhythm was apparently of sinus origin except for an occasional premature contraction.

Diagnosis.—(1) Post-rheumatic (inactive) myocardial damage.

(2) Cardiac enlargement (moderate).

(3) Mitral stenosis and insufficiency with auricular fibrillation.

(4) Class II b. (N. Y. Cardiac Clinics Classification).

The patient returned to work January 2, 1925, and my examination on February 3, 1925 seemed to confirm what he himself claimed—"I feel better than at any time since May, 1922." His weight was 120¼ pounds; blood-pressure, systolic, 144; diastolic, 74; pulse rate, 74; apical rate, 74, with no premature contractions heard. The liver was not palpable and no râles could be heard at the base of the lungs.

He continued at work daily until June 24, 1925, when the author was called to his house and found him in bed. On June 11th, because of the excessive heat and feeling that quinidin sulphate increased his perspiration, he had stopped this medication. On Saturday, June 20th, after a strenuous day, he suddenly felt weak with marked breathlessness and palpitation of the heart.

On examination on June 24th it was found that auricular fibrillation had returned, with an apical rate of 164 and a pulse rate of 68. Blood-pressure: systolic, 96; diastolic, 80. As he claimed he could not take the tincture of digitalis, he was given 1 dram of digital, and digital, 30 drops three times a day, was ordered.

On June 28th his heart rate was 88, pulse rate 88; blood-pressure: systolic, 100; diastolic, 80; but he stated: "I am beginning to get poisoned from digitalis; I feel the way I did for the two years I was on that drug." The digitalis was stopped and quinidin sulphate, 5 grains four times a day, was prescribed.

On July 7th, on arriving at the house, it was found that during the night sinus rhythm had returned. His apical rate was 120 and his pulse rate 120, with an occasional premature contraction. Blood-pressure: systolic, 110; diastolic, 88. The quinidin sulphate was reduced to 6 grains three times a day.

On July 8th the apical rate was 80, the pulse rate was 80, with no premature contractions noticed. On July 10th the apical rate was 70 and the pulse rate 70, with a sinus rhythm still present, and the dose of quinidin sulphate was reduced to 5 grains t. i. d. The patient returned to work on August 1, 1925, and has worked steadily, not missing a day.

Electrocardiographic Findings.—January 22, 1926: (1) Sinus rhythm, except for the two auricular premature contractions in Lead II and in Lead III.

(2) Right ventricular preponderance.

(3) Normal auriculoventricular conduction (P. R. interval 0.18 second).

On March 4, 1926 the patient weighed $119\frac{3}{4}$ pounds; apical rate, 76; pulse rate, 76; blood-pressure: systolic, 134; diastolic, 72.

L. B. = 11 cm. in the sixth interspace.

R. B. = 3.5 cm. in the fourth interspace.

The liver was not palpable and no râles could be heard at the bases of the lungs.

Case VI.—Mr. A. D., aged fifty-nine. Swiss. Clerk in wholesale drug firm.

Past Medical History.—Had smallpox as a child and typhoid fever when fourteen years old. When twenty years of age had a primary lesion of syphilis. From that time until the onset of his present illness: "I was never sick a day."

History, Present Illness.—In March, 1922 admitted to the wards of the Episcopal Hospital, Philadelphia, complaining of cough, breathlessness, and bilateral swelling of his lower limbs. He was placed at rest and on a limited diet and given tincture of digitalis, minims 15, t. i. d. His condition improved somewhat, but the edema of his lower limbs and moderate breathlessness never disappeared. After several months in a wheel chair and following what to him seemed a hopeless prognosis, he left the hospital against advice. The day after arriving home, September 18, 1922, he started for work and collapsed in front of the Pennsylvania Hospital.

Physical Examination.—Patient was a well-developed man, cyanotic, and definitely breathless. Temperature $99\frac{1}{5}$° F.; height 5 feet, 10 inches; weight 188 pounds. Blood-pressure: systolic, 156; diastolic, 90.

The teeth were evidently a possible focus of infection, the tonsils small and buried. There were visible, rapid, irregular,

cervical pulsations and a marked systolic heave to the precordium. The apex-beat was diffuse and heaving in the fifth and sixth interspaces, but no thrill could be felt.

L. B. = 15 cm. in the sixth interspace.

R. B. = 5 cm. in the fourth interspace.

P. M. B. = 6.5 cm. in the first interspace.

The rhythm was definitely that of auricular fibrillation with an apical rate of 148 and a pulse rate of 108 (pulse deficit, 40). A harsh systolic murmur could be heard at the apex, and at the base a long, low, diastolic murmur could be heard, transmitted downward toward the apex. Posteriorly at the bases of both lungs there was impairment to percussion, distant breath sounds, and diffuse subcrepitant râles. All of these were more definitely present at the right base. The liver was easily palpable 8 cm. below the xyphoid cartilage in the midline and somewhat tender. There was marked bilateral edema of both lower extremities.

Diagnosis.—(1) Arteriosclerotic (or syphilitic (?)) myocardial damage.

(2) Cardiac enlargement (marked).

(3) Aortic insufficienty(?) and mitral insufficiency (relative) with auricular fibrillation.

(4) Class 3 (on admission), progressing to class 2B (N. Y. Cardiac Clinics Classification).

Treatment.—September 18, 1922: He was placed at rest on a limited diet with a fluid intake of 1500 c.c. per day and given a stat. dose of 1 dram of tincture of digitalis and then 30 minims, four times a day.

On September 24th the apical rate was 88 and the pulse rate 88; the digitalis was reduced to 20 minims four times a day, and again on October 3d, to 15 minims t. i. d., and finally to 10 minims t. i. d. on October 5th, and he continued taking this amount of digitalis until leaving the hospital wards.

On October 11th at 12 noon he was given 3 grains of quinidin sulphate, and then 6 grains at 2, 6, 10, and 6, and 10 o'clock of the following day. After this last dose it was noticed that sinus rhythm had returned, with a marked improvement in his condition, according to the patient.

This patient has continued to attend our heart clinic to date, that is, over a period of almost four years, taking quinidin sulphate, 3 grains (in capsules which he puts up himself) t. i. d., and except for several weeks' rest in the hospital every six months, which we insist upon, he has not lost a day at work on account of any circulatory insufficiency.

Case VII.—Miss A. K., aged fifty-six. White. Engraver's helper in the United States Mint.

History, Present Illness.—Was admitted to the Pennsylvania Hospital on December 12, 1925 on Dr. G. W. Norris' service. She had been feeling perfectly well until January 1, 1925, except for frequent "winter colds." On this date she was riding in a trolley car and thinks her handbag struck her over the heart, as she suddenly began to have pain over this area; shortness of breath and a smothering sensation developed. Under her family physician's advice she gave up work and rested at home, "taking digitalis." On March 14th, while out for a walk, a sudden much more serious attack of breathlessness developed and she was confined to bed until May 28th. Upon getting up and being around the house for a week the symptoms continued to advance and she came to the hospital.

There has been no edema of the ankles, pain over the abdomen, and only a slight non-productive cough at times.

In the past, except for diphtheria in childhood, she claims to have been absolutely healthy. There was no true history of acute rheumatic fever, chorea, growing pains, or tonsillitis. The menopause occurred in 1924 and was apparently symptomless.

Except that her father "died of heart trouble and the mother of edema of the lungs" the family history was irrevelant.

The patient claims to have worked hard all her life and to have "assumed the responsibility for the whole family most of the time."

The *physical examination* on June 13, 1925 revealed the patient propped up in bed and definitely orthopneic (respiratory rate 46 per minute). Weight, 153½ pounds; temperature, 98⅗° F.; blood-pressure: systolic, 210; diastolic, 135.

The tonsils and teeth were not apparently foci of infection. There was quite marked cyanosis, and rapid, irregular, cervical pulsations were visible. A marked systolic heave to the precordium could be seen, but no thrills were felt. The apex-beat was forceful and diffusely palpable in the fifth interspace.

L. B. = 15 cm. in the fifth interspace.

R. B. = 4 cm. in the fourth interspace.

P. M. D. = 6 cm. in the first interspace.

The apical rate was 122 and the pulse rate 84 (pulse deficit 38). The rhythm was definitely that of auricular fibrillation. No murmurs could be heard.

Posteriorly, at the base of the right lung, there was definite impairement with distant voice and breath sounds. Many subcrepitant râles could be heard throughout the lungs anteriorly and posteriorly, but most numerous at the right base. The liver was somewhat tender with the lower edge easily palpable 14 cm. below the xyphoid cartilage in the midline. No edema of the lower extremities was demonstrable.

Diagnosis.—(1) Arteriosclerotic myocardial changes, with marked cardiac enlargement.

(2) Auricular fibrillation.

(3) Class III (N. Y. Cardiac Clinic Classification).

Laboratory Findings.—The urine was acid in reaction, with a specific gravity ranging between 1026 and 1010. A light to a heavy cloud of albumen with some light granular casts appeared on five examinations between June 13, 1925 and July 1, 1925. Following this no albumen and no casts were seen in four examinations. June 13th: Hemoglobin, 85 per cent.; red blood-corpuscles, 5,150,000; white blood-corpuscles, 9200. June 15th: Blood Wassermann negative. Blood chemistry, sugar 101 mg. per 100 c.c.; urea nitrogren, 16.2 mg. per 100 c.c.; creatinin, 1.3 mgm. per 100 c.c. June 21st: Phenolphthalein elimination, first hour, 55 per cent; second hour, 20 per cent

Treatment.—On admission the usual purgation, limited diet and rest in bed, with a fluid intake limited to 1500 c.c., was ordered. June 12th tincture of digitalis, 30 minims, four times a day, was ordered. On June 15th this was increased to 50 minims

four times a day, as the apical rate was still 106 and the pulse rate 98. The patient was much more comfortable, but auricular fibrillation was still present.

On June 18th strychnin sulphate, $\frac{1}{30}$ grain; nitroglycerin, $\frac{1}{100}$ grain, and caffein citrate, 1 grain, was begun three times per day. The apical rate was 116; pulse rate, 104; blood-pressure: systolic, 210; diastolic, 120.

June 19th, as the apical rate was 88 and the pulse rate 80, the digitalis was reduced to 35 minims four times a day, and daily thereafter a 5-minim reduction per dose was made, until, on June 21st, the patient was taking 25 minims four times a day. The apical rate was then 80 and the pulse rate 64, with a systolic blood-pressure of 200 and a diastolic of 114. The liver was palpable now only 7 cm. below the xyphoid in the midline.

On June 27th the apical rate was 74, the pulse rate 74, the blood-pressure: systolic, 180; diastolic, 100. On July 7th the digitalis was stopped and quinidin sulphate, 3 grains, were given morning and evening. On July 3d this was increased to three times a day, and on July 4th quinidin sulphate, 6 grains, were ordered three times a day. At this time the apical rate was 100 and the pulse rate 70. On July 5th 6 grains were given four times a day, and on July 7th these were increased to 9 grains four times a day.

On July 8th a return to sinus rhythm had occurred with an apical rate of 78 and a pulse rate of 78; blood-pressure: systolic, 187; diastolic, 100, so that the quinidin sulphate was reduced to 6 grains four times a day. On July 9th it was still further reduced to 6 grains three times a day, and on the 11th to 3 grains, three times a day. The patient was now allowed out of bed one or two hours twice a day, and on July 15th the apical rate was 72 and the pulse rate 72. On July 24th the patient returned home still taking quinidin sulphate, 3 grains three times a day, with a sinus rhythm and seemingly in comparative comfort.

Electrocardiographic Findings.—June 15, 1925: (1) Auricular fibrillation.

(2) Left ventricular preponderance.

July 1, 1925: (1) Auricular fibrillation.

(2) Left ventricular preponderance.

(3) Marked inversion of T-waves in Leads I, II, and III.

July 9, 1925: (1) Normal sinus rhythm.

(2) Left ventricular preponderance.

(3) Slight inversion of T-waves in Leads I, II, and III.

(4) Normal auriculoventricular conduction (P. R. interval, 0.20 second).

This patient during the past year has continued to take 3 grains of quinidin sulphate t. i. d., and missed very few days from work. She has at no time during the past year been confined to bed because of cardiovascular symptoms, and at present her rhythm is still of sinus origin.

Case VIII.—Mrs. M. C., Jr., aged fifty-two. White housekeeper.

This patient was first seen with Dr. Branson, of Rosemont, Pa., on November 25, 1924. Except for a history of chronic tonsillitis most of her life, the past medical history and family history were absolutely negative from the standpoint of her cardiovascular system. Six days before the author's first examination she had had a tooth extracted. That evening the patient became suddenly breathless and noticed that "the heart beat very rapidly and irregularly." Since that time the patient had been confined to bed on a limited diet and had been given sodium bromid. The author's examination revealed a well-developed female, well above the average intelligence, definitely orthopneic (respiratory rate 26 per minute), and definitely cyanotic. Weight, 148 pounds; blood-pressure: systolic, 98; diastolic, 68. Rapid, irrgeular, cervical pulsations were visible and there was a slight but definite systolic heave to the precordium. The apex-beat was easily palpable in the fifth interspace and somewhat overactive. No thrills were felt.

L. B. = 13 cm. in the fifth interspace.

R. B. = 4 cm. in the fourth interspace.

P. M. D. = 5.5 cm. in the first interspace.

The rhythm was typically that of auricular fibrillation with an apical rate of 118 and a pulse rate of 68. The first sound at

the apex was short and snappy, a definite short systolic murmur could be heard at this area, and with the patient lying on the left side a short diastolic murmur could be heard during the longer diastoles, but no presystolic element was heard.

At the right base posteriorly there were numerous subcrepitant râles, but otherwise the lungs were apparently negative. The liver was just palpable about 3 cm. below the right costal margin and very slightly tender. There was no demonstrable edema of the lower extremities.

Treatment.—At the author's suggestion the patient was given 3 grains of the Upshur-Smith pulverized digitalis, t. i. d., for twenty-four hours, and this was reduced 1 grain every other day until at the end of six days the patient was taking pulverized digitalis, 1 grain, t. i. d. On December 1st the apical rate was 80 and pulse rate 80. The patient was symptomatically much improved, but complained that "the green capsules nauseate me." No râles were demonstrable at the right base and the liver was only just palpable under the right costal margin, with no tenderness. The murmurs were as described above and auricular fibrillation was still present.

On January 8, 1925 patient was moved to the Pennsylvania Hospital, where the physical examination was practically the same as on December 1, 1924—the patient still taking pulverized digitalis, 1 grain t. i. d., but bitterly complaining of its nauseating effects, although there had not been any actual vomiting.

Electrocardiographic Interpretation.—January 9, 1925: Tracings show a typical arhythmia of the type of auricular fibrillation; although the Q waves in Lead III are definitely deeper than normal there is no definite evidence of preponderance of either ventricle. The T waves appear to be diphasic in Leads II and III (probably the result of digitalis therapy). The ventricular rate averages about 88 per minute.

At noon, January 10th, patient was given quinidin sulphate 3 grains and the digitalis was stopped. The quinidin was repeated every fourth hour during the twenty-four hours. On January 12th the quinidin sulphate was increased to 6 grains

every fourth hour, and this was continued until January 15th, when the dosage was increased to 9 grains every fourth hour. On the morning of January 19th sinus rhythm had apparently returned with an apical rate of 88 and a pulse rate of 88.

Electrocardiographic Interpretation.—January 19, 1925: Tracings show a normal sinus rhythm, with an average auricular and ventricular rate of 88 per minute. There is no change in the character of the ventricular complexes from those in the tracings made January 9th. There is no apparent preponderance of either ventricle and no delay in conduction time as the P–R. interval averages about 0.16 second and the Q. R. S. complexes about 0.08 second. The T-waves in Lead III are somewhat diphasic (possibly a persistence of the digitalis effect).

On January 20th sinus rhythm was still maintained with the blood-pressure 128 systolic, 70 diastolic. The apex-beat was palpable in the fifth interspace with no thrills demonstrable.

L. B. = 12 cm. in the fifth interspace.

R. B. = 4 cm. in the fourth interspace.

A definite short systolic murmur with a longer diastolic was heard at the apex. Digitalis therapy was not resumed, but the patient has been kept on quinidin sulphate, 3 grains t. i. d., to date.

During March, 1926 the patient was again examined by the author, at which time the physical findings were practically the same as on January 20, 1925. The patient and her family physician felt that she had practically returned to that stage of cardiovascular efficiency which she had had before the onset of her auricular fibrillation in November, 1924.

Case IX.—Mr. C. M., aged thirty-five. White. Railroad freight brakeman.

History, Present Illness.—Was admitted to the Pennsylvania Hospital on December 7, 1925, stating that on October 7, 1925 he first visited his family physician complaining of shortness of breath on slight exertion. This symptom had been present for several months, but there had been no precordial pain, palpitation, headache, or vertigo. A non-productive cough, worse at

night, had bothered him lately. No gastro-intestinal symptoms were complained of.

At the age of thirteen years he had a severe attack of rheumatic fever; all his joints "were wrapped in bandages confining me to bed for two months." Except for pneumonia and pleurisy in 1921 he had had no other illnesses except "winter colds almost every year."

Although a married man for six years, his wife had had no pregnancies.

He had always worked at laborious occupations, *i. e.*, a prize fighter, a machinist and finally a freight brakeman. He never smoked more than 10 cigarettes a day nor gave a history of alcoholic excess.

The physical examination on December 9, 1925 revealed the patient lying flat in bed, but with definite breathlessness (respirations 24 per minute); temperature, $98\frac{4}{5}$° F.; height, 5 feet, 9 inches; weight, 192 pounds; blood-pressure: systolic, 105; diastolic, 60.

The tonsils were buried and cryptic. The teeth were not apparently a focus of infection. There was slight but definite cyanosis, and visible, rapid, irregular, cervical pulsations could be seen. No true systolic heave to the precordium could be made out, but the chest was of a definitely emphysematous type. The apex-beat was palpable in the fifth and sixth interspaces, but no definite thrills were felt.

L. B. = 15.5 cm. in the sixth interspace.

R. B. = 4.5 cm. in the fourth interspace.

P. M. D. = 5.5 cm. in the first interspace.

The apical rate was 116 and the pulse rate 104 (pulse deficit 12); the rhythm was definitely that of auricular fibrillation. The first sound at the apex, especially with the more forceful systoles, had a definitely snappy quality. There was a harsh systolic murmur at the apex, and while lying on the left side, especially during the longer diastoles, a short diastolic murmur could be heard.

Posteriorly, at the bases of both lungs, but more definitely at the right base, numerous inspiratory subcrepitant râles of the

congestive type could be heard. The liver, although not tender, was easily palpable 8 cm. below the xyphoid cartilage in the midline.

Diagnosis.—1. Post-rheumatic (inactive) myocardial damage.

2. Cardiac enlargement (moderate).

3. Mitral stenosis and insufficiency with auricular fibrillation.

4. Class III (N. Y. Cardiac Clinics Classification).

Laboratory Findings.—Three urine examinations were all acid in reaction, with a specific gravity ranging between 1022 and 1005. A faint trace of albumen was present in the first two examinations, but no casts or blood-cells were seen. Blood Wassermann reaction was negative; hemoglobin, 95 per cent.; red blood-cells, 4,450,000; white blood-corpuscles, 7050.

Treatment.—On admission the usual purgation, limited diet, and rest in bed was ordered. A preliminary dose of 1 dram of tincture of digitalis was given, followed by 20 minims three times a day from December 7th to December 11th. On this last date the apical rate was 90 and the pulse rate was 80, while auricular fibrillation was still present. Tincture of digitalis was stopped and quinidin sulphate, 3 grains, were ordered five times in twenty-four hours (at 6, 10, 2, 6, and 10 o'clock). This was continued until December 14th (three days), when the dose was increased to $4\frac{1}{2}$ grains at the same intervals. On December 15th tincture of digitalis in 20-minim doses t. i. d. was again started in addition to the quinidin sulphate, as the apical rate was 100 and the pulse rate 94, with auricular fibrillation still present. On December 17th the quinidin sulphate was increased to 6 grains five times in the day, given as above, and on December 21st, to 9 grains five times in the day. The apical rate on this date was 81, and the pulse rate was 81, but auricular fibrillation was still present. On December 22d the apical rate was 90 and the pulse rate 90, and there had been a return to sinus rhythm, so that the dose of quinidin sulphate was reduced to 6 grains five times in the day. On December 28th, with the patient up and around the wards, the apical rate was 80 and the pulse rate 80, with sinus rhythm

TABLE 1

COMPLICATION OF CASES OF AURICULAR FIBRILLATION[1] REPORTED TREATED WITH QUINIDIN

Authors.	Number treated.	Reversions to normal rhythm.	
Arnell	9	4	
Arrillage, Waldrop, and Guglielmetti	14	9	
Benjamin and von Kapff	27	18	
Bock	35	16	
Boden and Neukirch	17	6	
Burwell and Dieuaide	16	14	
Clerc and Deschamps	24	12	
Drury and Ilescu	13	6	
Ellis and Clark-Kennedy	7	5	
Euster and Fahr	2	1	
Faber	2	1	
Frey	50	21	
Floystrup	2	2	
Haass	44	27	
Hamburger and Priest	18	11	
Hart	15	5	
Hewlett and Sweeney	12	6	
Jenny	18	17	
Klewitz	13	1	
Leschke and Ohm	1	1	
Levy	25	11	
Lian and Robin	4	3	
Oppenheimer, Mann, and Felberbaum	56	25	
Romberg	22	17	
Sappington	1	1	
Schott	2	2	
Smith	12	6	
Stroud	42	27	
Van Bergman	9	6	
Van Tilburg	10	8	
White, Marvin, and Vike	75	51	
Wilson and Hermann	1	1	
Wisser	11	4	
Wolferth	12	7	
Wybauw, Dumont, and Joos	27	14	
Total	648	366	(56.4%)

[1] For references mentioned in this table see our reference No. 9—Burwell and Dieuaide—Archives of Internal Medicine, April, 1923, vol. 31, pp. 518–526.

still present. On December 30, 1925 the quinidin sulphate was reduced to 4.5 grains t. i. d., and the patient was sent home.

Electrocardiographic Findings.—December 8th: 1. Auricular fibrillation.

2. Right ventricular preponderance.

December 22d: 1. Normal sinus rhythm.

2. Low-grade heart-block (P-R interval 0.28 second).

3. Right ventricular perponderance.

SUMMARY

A preliminary report on 134 patients with auricular fibrillation observed over a period of five years would indicate that there is a definite place for quinidin sulphate in the tratment of such patients. In support of this conclusion certain cases are reported and special reference is made to the work of Bloomguard and Weiss.[11] Of the 42 patients in our series given quinidin sulphate, 27, or 64 per cent., had a successful return to sinus rhythm.

REFERENCES

1. Levine, S. A., and Wilmaers, Albert: Boston Med. and Surg. Jour., February 26, 1925.
2. Reid, William D.: Jour. Amer. Med. Assoc., December 9, 1922, vol. 79, pp. 1974, 1975.
3. Von Frey, W.: Berl. klin. Wchnschr., 36, 850, 1918.
4. Von Frey, W., and Hagemann, F.: Ztschr. f. d. ges. exp. Med., 25, 290, 1921.
5. Haass, H.: Berl. klin. Wchnschr., 58, 540, May 23, 1921.
6. Wilson, F. N., and Hermann, G. R.: Jour. Amer. Med. Assoc., 78, 865, March 25, 1922.
7. Cohn, A. E., and Levy, R. L.: Abstr., Jour. Amer. Med. Assoc., 78, 1839, June 10, 1922.
8. Lewis, Thomas: Amer. Jour. Med. Sci., 163, 781, June, 1922.
9. Burwell, C. Sidney, and Dieuaide, Francis R.: Archives of Internal Medicine, April, 1923, vol. 31, pp. 518–526, vol. 31, No. 1.
10. Korns, Horace M.: Archives of Internal Medicine, January 15, 1923, pp. 40, 41.
11. Bloomguard and Weiss: To be published in the Transactions for 1926 of the American Association for Clinical Investigation and the American Association of Physicians.

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MALNUTRITION. THE MODERN PEDIATRIC PROBLEM

So much has been written of late concerning malnutrition that one hesitates to add another contribution. The problems involved are so many sided and the cure often is so difficult that the last word will not be said for many years. It is also well to note that the condition sometimes is given an undue amount of weight in our characteristic enthusiasm over a comparatively new subject, and it behooves us therefore to maintain our poise in the face of much popular clamor for relief.

"Malnutrition" is a term usually applied to children from two years of age to puberty, whose weight is below the normal for height and in whom both weight and height may or may not be below the normal for age.

As a rule, the term is used only to designate that form of deficiency in weight which is not due to any definite disease. Active tuberculosis, diabetes, chronic pyelitis, and, in fact, practically all diseases except certain endocrine disturbances and those with edema, cause more or less loss of weight, but malnutrition as a term is reserved for that state which has more subtle and less obvious causes.

The term "infantilism" is used in a different sense. This indicates a failure of the child to grow rather than mere discrepancy between weight and height, and again, usually is dependent upon definite disease.

The diagnosis of simple malnutrition obviously must be made only after the most careful exclusion of disease, especially

tuberculosis. Granting that none can be found, we should next determine the degree of malnutrition as a starting-point for future comparisons.

Authorities are not yet in full accord as to normal standards for nutrition. All are agreed that the age-weight ratio is misleading. For practical purposes the height-weight ratio or the sitting height-weight ratio is more reliable. In addition, and equally important, is the estimation of bodily vigor. This can be determined only by careful physical examination with the child's clothes removed.

A child with well-developed muscles, a good chest expansion, who never tires under average circumstances, who sleeps well and whose disposition is agreeable, need not become an object of solicitude because he happens to be somewhat underweight.

It should also be remembered that children with small bones, especially of the legs, may be below average weight and yet quite healthy, since bone comprises such a large percentage of the total body weight. On the other hand, large-boned children may be really malnourished without showing much weight deficiency.

In estimating degrees of malnutrition the table of Emerson and Manny (page 357) may be used.

Variations within a 5 per cent. limit of deficiency commonly are disregarded. When weights are from 5 to 10 per cent. or more below normal we are dealing with a more severe degree of deficiency which demands investigation and correction if possible.

In general, it will be found that anorexia or at least a capricious unequal appetite is present in most instances of malnutrition. Rarely will that child be found much underweight who uniformly eats three good balanced meals a day.

Another general rule is that very thin children are apt to be overactive. It is axiomatic to say that all healthy children are active. Lethargy in childhood almost invariably is pathologic. To find a thin child persistently overactive, therefore, is rather reassuring, since it usually presupposes freedom from actual disease. The case of the overactive child who tires easily is, as Kipling says, another story.

Boys:				Girls:			
Age, years.	Height, inches.	Average weight for height, pounds.	7 per cent. under-weight, pounds.	Age, years.	Height, inches.	Average weight for height, pounds.	7 per cent. under-weight, pounds.
1	29.50	*21.5	20.0	1	29.0	*20.0	18.5
2	33.50	*26.5	24.5	2	33.0	*25.0	23.5
3	36.50	*32.0	30.0	3	36.0	*30.0	28.0
4	39.0	*35.0	32.5	4	39.0	*34.0	31.5
5	41.50	39.0	36.5	5	41.5	38.0	35.5
6	44.0	44.0	41.0	6	44.0	42.0	39.0
5½–6½	46.0	48.0	44.5	5½–6½	45.0	45.0	42.0
6½–7½	48.0	53.0	49.5	6½–7½	47.0	50.0	46.5
7½–8½	50.0	58.0	54.0	7½–8½	50.0	58.0	54.0
8½–9½	52.0	64.0	59.5	8½–9½	52.0	64.0	59.5
9½–10½	54.0	71.0	66.0	9½–10½	54.0	71.0	66.0
10½–11½	56.0	78.0	72.5	10½–11½	56.0	79.0	73.5
11½–12½	58.0	85.0	79.0	11½–12½	58.0	89.0	83.0
12½–13½	60.0	94.0	87.5	12½–13½	60.0	101.0	93.5
13½–14½	63.0	111.0	103.0	13½–14½	62.0	114.0	106.0
14½–15½	65.0	123.0	114.5	14½–15½	63.0	118.0	109.5
15½–16½	67.0	133.0	123.5	15½–16½	64.0	121.0	112.5
16½–17½	68.0	139.0	129.5	16½–17½	64.0	121.0	112.5

* Without clothes.

To consider more specifically the causes of malnutrition it will usually be found that these children will fall into one or more of the following classes as designated by Emerson:

1. Those who have received insufficient or poorly balanced food or whose eating habits are improper.

2. Those who have had poor hygiene, insufficient physical rest and sleep, or fresh air and sunshine.

3. Those who have physical defects.

4. Neurotic or neuropathic children.

To these I would also add a fifth class:

5. Those who give a history of a familial tendency to leanness.

1. If the requirements for protein, fat, carbohydrate, salts, water, vitamins, and calories are met, if the food is properly

selected and prepared, and if sufficient intervals between feedings are observed, satisfactory gain can be secured for the majority of children.

One habit very common to children between four and fourteen is that of "bolting" their food. Usually this is due to their desire to get through with the meal and to resume their interrupted play. The remedy is to insist that a certain time be spent at the table and, for severe types of malnutrition, that a rest period of fifteen to thirty minutes be taken before and after the midday and evening meals.

The reverse of too rapid eating sometimes is seen in the case of the child who "dawdles" over its meals, consuming as much as an hour or more. This may leave a shorter interval for digestion than is desirable and is apt to diminish appetite.

Toys and games should never be combined with meals. The practice of telling stories of animals, for example, so that the child will emulate their eating habits, may be permissible in selected cases, but the danger is that the child's imagination may be so stimulated that it forgets the main duty of mealtime, which is to eat.

The question of what comprises a suitable allowance of food is open to some difference of opinion. Probably Holt's table (page 359), based upon the amount of food actually consumed by healthy children, gives a reliable index to nutritional needs.

Of the total calories, approximately 15 per cent. should be derived from protein, 35 per cent. from fats, and 50 per cent. from carbohydrates. The food allowance should include from 15 to 20 ounces of milk a day, taken as such, in addition to the amount used for cooking. Green leafy vegetables, stewed and raw fruit, whole-grain cereals, a starchy vegetable, whole-wheat bread, butter, one egg, and a moderate amount of meat should be included in every day's allowance. At least one glass or, preferably, two glasses of water should be taken daily between meals.

Apart from anorexia for food in general, the greatest difficulty lies with children who like a few articles to the exclusion of everything else. Milk is the chief offender, and in view of the extensive propaganda in favor of milk as food, it is small wonder

CALORIC REQUIREMENTS AT DIFFERENT AGES

(Holt[1])

Age.	Calories per		Age.	Calories per	
	Pound.	Kilo.		Pound.	Kilo.
3 months.	55	120	9 years.	36	80
6 months.	55	120	10 years.	36	80
9 months.	50	110	11 years.	36	80
12 months.	45	100	12 years.	36	80
2 years.	42	93	13 years.	36	80
3 years.	40	88	14 years.	36	80
4 years.	38	84	15 years.	36	80
5 years.	37	82	16 years.	34	75
6 years.	36	80	17 years.	31	69
7 years.	36	80	18 years.	28	62

[1] Food, Health, and Growth.

that the mother encourages the child to form the milk habit. Owing to its so-called buffer substances which absorb the hydrochloric acid of the gastric juice as a dry sponge absorbs water, a plentiful supply of milk taken at the beginning of a meal is well calculated to satisfy any but the most unusual degree of hunger. In breaking the milk habit the first step is to interdict milk absolutely for a few days until the child has learned to take other foods. Later it should be permitted only with breakfast and supper so as to favor the consumption of the more important and varied meal—the dinner. Sweets, such as candy, cake, or sweet desserts, should be given only at the conclusion of the meal and only in small quantities. Nothing is easier to acquire than a taste for sweets, and nothing destroys the appetite, especially for vegetables, so quickly as sweets. On the other hand, there can be no objection to a reasonable amount, provided the best part of the meal has been eaten. It is a good general rule also that eating between meals should be forbidden.

2. There are many children today who receive an approved diet, whose hygienic habits are unimpeachable, and who nevertheless suffer from malnutrition. Often the fault lies in their

unceasing physical activities which rob the calories destined for growth. At the beginning of the campaign against malnutrition part of the prescribed formulæ was the mid-morning and often the mid-afternoon luncheon, usually composed of milk and crackers. These may have their place under certain conditions, but it was found that they often failed entirely to produce any permanent or material gain in the class of overactive children. Incidentally, milk between meals often materially diminishes the appetite for the next meal.

For the active children the great need is for rest periods of from one-half to one hour once or even twice a day; not only to diminish the actual amount of exercise but also to break up the nervous strain of continuous exciting play.

One of the most important rules for health is the continuance of the rest hour after the child has become too old to take its daily nap. Until the demands of school prevent, every child should have its midday rest with outer clothes and shoes removed and the room ventilated as at night. Toys and games should be forbidden. Sleep cannot be forced, but physical rest can be insisted on. Once the habit is allowed to lapse, many self-willed children resent the attempts to reinstate it.

Sufficient sleep at night is another rock on which many families almost split. The father demands the opportunity to play with the child after he returns from work, forgetful both of the child's welfare and the mother's nerves which have often been severely strained by the attempts at disciplining the child throughout the day. For the child to get to bed early is not only good for it, but is a definite relief to the mother. Circumstances alter cases, to be sure, but in general, one can prescribe a sleep schedule as follows:

Age.	To be in bed at	Hours of sleep.
2 to 6 or 7 years, called the preschool period	7 P. M.	11 to 12
6 or 7 to 12 years	8 P. M.	10 to 11
12 to 15 years	9 P. M.	9 to 10

Exceptions should be made only for very good reasons and, during the school year, on nights which do not precede school days.

Fresh air scarcely needs a champion nowadays, but the difficulty in temperate and northern climates is to overcome the fear of cold air. Again, it is largely a matter of habit. The child accustomed to a day spent out-of-doors in autumn can usually continue the habit in winter, modified sufficiently to prevent thorough chilling. Cold, *per se*, rarely causes illness. Infection plus chilling may have bad results. If opportunities for infection can be avoided, cold will lose most of its terrors for the overcautious mother.

Nothing apparently can take the place of direct sunlight in favoring the proper growth and development of children. Provision for this should be made in the life of every child, and the daily sun-bath should be prescribed for every child under three when the weather conditions permit. There is need for care as to overexposure at the beginning of these treatments and during the extreme heat of summer, but in the latter instance a judicious admixture of sunlight and cool (not cold) bathing will be found to be of the greatest value.

3. Some important physical defects can usually be found to explain malnutrition when all other errors in diet and hygiene have been corrected. The most common are enlarged and infected tonsils and adenoids, or infected paranasal sinuses. Properly these come under the head of disease, and yet they may cause no obvious symptoms. They damage the child's organism, probably by reason of toxic absorption, although the mere presence of greatly enlarged tonsils and adenoids with the attendant low-grade inflammation and hypersecretion and interference with proper breathing and oxygenation may effect appetite and consequently nutrition.

Other defects may be found in the gastro-intestinal tract. Gastroptosis and gastrectasis, with various defects in the size and position of the intestine, may exist for a time without causing symptoms, but sooner or later will affect digestion and the absorption of food. These anatomic conditions are accompanied by more or less sagging and protrusion of the abdominal wall, giving rise to the so-called fatigue posture. On the other hand, the fatigue posture more commonly results from malnu-

trition, possibly dating back to early rickets, and may exist without gross deformities of the gastro-intestinal tract. The weakening of the abdominal wall permits dragging on the mesentery and interference with the circulation, and hence is at once a cause and an effect of malnutrition, a true vicious circle.

True anatomic defects usually produce vomiting or obstinate constipation, or both. Roentgenologic studies of the gastro-intestinal tract occasionally will reveal surprising results. Both for these cases and for those with the simple sagging abdomen the essential treatment is by some form of support. The natural means is to improve the tonus of the abdominal muscles. Even with very small children, three or four years of age, a great deal can be done by systematic daily exercises. The most useful are: (1) To flex the extended thigh and leg on the abdomen while lying flat on a table or the floor, first raising the right, then the left, then both legs, and repeating each movement ten to twenty times, and (2) while lying flat with arms folded on chest to raise the body to a sitting position with the legs fully extended; (3) standing erect to pull the abdomen in as far as possible by forced contraction of muscles and then slowly to relax. The child should also be taught to hold the abdomen in as a general habit of posture. Other forms of exercise can be devised, but too many are as bad or worse than none. It must never be forgotten that fatigue posture means general as well as local fatigue. The child's overactivities must be curtailed before we can safely impose extra work upon the abdominal musculature, *per se*.

In severe cases and in those who will not co-operate, some form of mechanical abdominal support may be used. This should always be supplemented by exercise as soon as possible and should not be worn too long. Probably this support acts merely to restore the normal intra-abdominal tension, since it is impossible by any feasible support to restore the gut or stomach to its normal position.

Badly decayed teeth are rarely found now among the children of intelligent people, except in the case of the spoiled child who refuses to bear with the attentions of the dentist. Bad

teeth are harmful because they interfere with proper mastication as well as from the absorption of, or swallowing, toxic material. Other causes of deficient mastication are dental malocclusion and nasal obstruction.

Among the rarer types of physical defects are cleft palate and nasal polypi. It may also happen that orthopedic deformities, such as club-feet or fallen pronated arches, may cause such physical exhaustion as to interfere with the child's nutrition. Any physical handicap acts thus in an indirect way, such as defective vision.

4. The well child who will not eat seems to be a modern product—at least one finds no mention of them in the older literature, while they exist in large numbers today. Probably both heredity and environment are at fault, for we find usually that one or both parents are neurotic and that the child lives in what might be called a neurotic environment; that he has never been taught moral control or that his training has been based on a system of implanted phobias, with constant nagging to the point that the child on general principles rebels at all orders.

The history is usually somewhat as follows: a child, usually an only child of two or three years of age, will begin to lose interest in its meals. The mother at once becomes alarmed and institutes various measures to compel the child to eat, begging, bribery, cajolery, or intimidation—repeated at each meal—ad nauseum. Very often attempts to force feeding induce the child to vomit the food. Perversity is an underlying attribute of all of us more or less, and in the child it exists uncontrolled by reason. To stimulate perversity nothing is better calculated than the constant nagging at meals. In a few weeks the mother is a nervous wreck and the child well set in its dislike for everything pertaining to meal-time—a condition of true negativism.

Another situation is created by overzealous parents in the case of a child who is of the hysteric type. With these children the great desideratum is attention, they crave the joy of being in the limelight. The story is told of the anxious parents who consulted a pediatrist in reference to their child who would not eat without a great amount of exhortation. The physician advised

that they simply place the food before the child without any comment, and pay no further attention to him. At the first attempt, the child made his usual objections to eating, and the parents quietly ignored him and went on with their conversation about other matters. After a few minutes the boy asked: "Aren't you going to make any fuss about my eating?" The moral of this is too obvious to need comment.

A third type of child may be described as hypersensitive. As a result of some emotional conflict, he loses his appetite and consequently stops gaining or loses weight. Veeder describes the instance of a boy of eight in which the fault partook of an inferiority complex. Naturally timid, he was constantly teased and plagued by the other children at school until it had an effect upon his whole disposition. The treatment in this case was to arouse interest in the development of muscles and in learning to handle himself physically. Instead of being put at rest he was given exercise, and as a result gained 12 pounds in a few weeks.

The majority of cases of anorexia in the nervous type of children begins at a time when their minds are the most active. It would seem that the excessive unregulated mental stimuli may destroy the desire for food very much as excessive nervous strain in adults sometimes destroys appetite.

It is noteworthy, however, that appetite improves when school begins. Apparently this contradiction can be explained by the fact that in the preschool days the mind is acting in a more or less chaotic fashion, as new impressions are received and ideas are formed extemporaneously, as it were. When school begins the mind is forced to act, for part of the time at least, in a more orderly and co-ordinate manner.

Other factors, of course, are concerned when children go to school, chief among which are the changes of environment, the familiarity which is acquired of the ideas, ways, and habits of other children, and the acquisition of the herd instinct—what other children do, the individual child is apt to copy. The significance of this can be appreciated when we realize that first children and only children are apt to be more benefited in their

eating habits by school training and association than the later children in large families.

In the most rebellious cases it will usually be found that the child's exaggerated sense of his own importance, fostered by over-zealous and over-solicitous parents, is the keynote in etiology. While only children are the special victims of this faulty environment, yet even children in large families are not immune, for in the latter case there is apt to be one especially favored for one reason or another—the pet—on whom is showered the whole family's special attentions. If anorexia exists among the group the pet or the tyrant, whichever way one chooses to put it, will almost always be the sufferer.

5. Finally, we come to the class of children who show no evidence of any gross defect or faulty environment and yet who will not gain. Usually, we will find that one or both sides of the family will show similar instances of leanness. Sometimes it is lifelong, but often it only lasts until middle age when the average adult begins to put on weight. In such instances, if the child is well and happy, we need have no especial concern about his failure to gain rapidly, provided he eats a reasonable amount and provided he at least gains something. Stationary weight cannot be disregarded over a long period of time since it is the equivalent of loss of weight in adult life, and in every instance of malnutrition the invariable rule should be to advise re-examination at least three or four times a year so as to detect potential disease in its incipiency. It is also true that periods of slow gain or stationary weight occur without obvious cause or with very slight cause, such as teething. As a rule, also, the fall and winter months show less gain than the spring and summer.

In the treatment of malnutrition, therefore, we first eliminate the presence of actual disease and then investigate minutely the dietary and other habits. Such inquiries should not be made in the hearing of the patient, if anorexia exists, since so many of these children belong to the neurotic class. As a basic rule, also, discussion of the child's eating habits in his hearing should always be omitted at his home. The danger of exaggerating his ego or of stimulating negativism is too great.

The meal-time should either be a pleasure or a duty. To make it a pleasure requires a cheerful attitude on the part of the adults and a freedom from criticism or bad suggestion. How often parents implant a dislike in the child's mind by saying that they themselves never liked and never could or would eat such and such food. The child is learning to eat just as he is learning to live; certainly no discouragement should be offered to his selection of a wide choice of foods. If the meal-time must become a duty, the less said about it the better; it should become part of the daily program—irksome perhaps, but necessary—just as brushing one's hair or teeth.

In general, it is wise to eliminate all eating between meals and to reduce milk to not more than 20 ounces a day, given at breakfast and supper after the completion of the meal. Both rich foods and sweets should be reduced to a minimum or eliminated entirely. Water drinking between meals must be encouraged. All foods should be well salted and should be given in small quantities so as to encourage the child to ask for more, rather than to be discouraged by the sight of an oversupply. Withdrawal of the privilege of eating with the family sometimes is effective, and deserts should be given only after the child has eaten a satisfactory meal. If the mother is highly neurotic some one else should feed the child, and it is astonishing what a change takes place when a competent nurse is placed in charge. The child also should be encouraged to feed itself. Under no circumstances should it be permitted to dominate the situation. Callous indifference is far better than sentimental overattention. Firmness without nagging usually will work a cure. In children who are seriously deficient in weight or in whom it is not easy to rule out the presence of actual disease, a preliminary rest-cure in bed is valuable. Often it will be found that appetite returns while they are resting. This usually is a clear indication that overexertion was at the bottom of the appetite defect. In other cases it is well to secure a new type of régime or a change of scene and air at the beginning of treatment.

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NON-DIABETIC GLYCOSURIA*

THE study of non-diabetic glycosuria has been stimulated greatly during the past few years. The discovery of relatively simple micro methods for the determination of blood-sugar has enabled us to differentiate several types of glycosuria.

Non-diabetic glycosuria may be divided into those cases with a normal threshold for glucose and those with an abnormally low threshold, the threshold being that concentration of the blood-sugar above which sugar appears in the urine.

The cases with a subnormal threshold may be divided into renal glycosuria and cyclic renal glycosuria. Renal glycosuria was considered a rare anomaly until the last decade, since when many cases have been found because of the ease with which the blood-sugar concentration can be made.

Renal glycosuria, like the other types of glycosuria which I shall discuss, often is discovered during a routine examination or during a life insurance examination. The findings in a typical case of renal glycosuria are: the constant presence of a small amount of sugar in the urine, usually 10 grams or less per day, which is unaffected by diet, and the absence of the usual symptoms of diabetes, such as thirst, polyuria, and loss of weight and strength. The diagnosis is made, however, by the discovery of an unusually low threshold for glucose. Such a patient has a normal or subnormal fasting blood-sugar with glycosuria. In both types of renal glycosuria the curve of blood-sugar after the ingestion of 100 grams of glucose does not go above .15 or .16

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per cent., and at the end of two hours is at or below the fasting level.

The cause of renal glycosuria has not been determined. In the earlier literature on this subject the statement is frequently found that a certain amount of kidney disease is associated with this condition. On the other hand, one sees the statement that when nephritis develops the glycosuria disappears. The latter is certainly the logical sequence in view of our present knowledge concerning nephritis and renal function. It has been shown by Richards[1] that the glomeruli excrete glucose and the tubules reabsorb it. A defect in the tubular function might thus explain the appearance of glucose in the urine in the absence of any elevation of blood-sugar; this would in effect bring about a lowered threshold and would explain the picture called renal glycosuria. Renal glycosuria, however, does not occur in what is commonly accepted as tubular nephritis or nephrosis.

Usually there are no subjective symptoms associated with renal glycosuria. The absence of diabetic symptoms frequently aids in the differential diagnosis of the two conditions. One occasionally finds cases of renal glycosuria that have polyuria, thirst, weakness, and loss of weight. Such cases have been reported by Holst[2] in 23 per cent. of his series; in all, however, blood examinations and the subsequent course of the cases showed them to be benign glycosuria.

The amount of glucose in the twenty-four-hour collection of urine in cases of renal glycosuria usually is less than 10 grams, and this amount, as a rule, is uninfluenced by diet. There are cases, however, in which the glucose in the urine reaches a concentration as high as 6 per cent., the total output for twenty-four hours in a few reported cases being as great as 100 grams. I[3] reported a case of this type in the Clinics of North America, several years ago. This patient, although he eliminated as much as 75 grams of glucose in twenty-four hours, continued to have an unusually low fasting blood-sugar. He had a blood-sugar concentration of .06 per cent. and a concentration of glucose in the urine of 2.5 per cent. after fasting forty-eight hours. The glycosuria in this case was discovered in 1918 during a routine

examination; when last seen, about a year ago, the patient appeared to enjoy good health, but continued to have the very low fasting blood-sugar and sugar in the urine. His glycosuria was influenced by diet.

Cyclic renal glycosuria is a type of benign renal glycosuria in which the glycosuria appears only after carbohydrate has been taken. In these cases one finds that at the fasting level of blood-sugar the urine is free of glucose, but contains it after the blood-sugar concentration has risen above the threshold of the individual, which threshold, however, is below .14 per cent.

Diagnosis.—As I have stated above, benign glycosuria is discovered usually during a life insurance examination, or during a routine examination. It is most important to recognize this type of glycosuria because of the difference in the treatment and outcome. The recognition of renal glycosuria is made by finding a fasting blood-sugar concentration of .11 per cent. or less, with glucose in the urine, and, as a rule, the absence of subjective symptoms. Mild diabetes occasionally is difficult to differentiate from this condition because there may be no subjective symptoms and a threshold below normal; as a rule, however, a mild, untreated case of diabetes has a fasting blood-sugar above .12 per cent. Treated cases of diabetes may have a fasting blood-sugar concentration within normal limits. The determination of the glucose tolerance of the patient often aids in the differential diagnosis. In non-diabetic glycosuria one obtains a normal blood-sugar curve, while in diabetes the blood-sugar concentration often increases considerably above normal and there is a delay in returning to the fasting level.

Richardson and Ladd[4] and others have shown in calorimetry studies that a patient with renal glycosuria is able to burn carbohydrate as a normal person does. Their work would indicate that in renal glycosuria there is no impairment in the function to burn and store glucose such as one finds in diabetes.

Prognosis.—The main question in prognosis is whether a case or renal glycosuria eventually becomes diabetic. This is very doubtful. Holst recently has stated that the cases of renal

glycosuria reported in the literature as having become diabetic have not been proved in a sufficiently convincing manner. This view is strengthened by the fact that most cases are discovered in young or relatively young people, which is the time of life when diabetes is progressive and most likely to become severe. Renal glycosuria has been discovered in families where one or more members suffered from diabetes. This might suggest that there may be a relationship between the two conditions.

Treatment.—The management of a case of renal glycosuria consists in allowing the individual to lead a normal life, eliminating in some cases foods very rich in carbohydrates. The urine and blood should be examined at fixed intervals to rule out any possible progression or change into diabetes if such occurs.

The other type of non-diabetic glycosuria that one finds in the routine examinations of apparently well people is periodic glycosuria with a normal threshold.

The glucose is detected in the urine usually in specimens voided after taking carbohydrates. These patients are free of subjective symptoms. If 100 grams of glucose are given to such individuals and the blood-sugar concentration determined every half-hour for two hours, it will be found that the blood-sugar concentration may rise to approximately .2 per cent. within the first hour and sugar will appear in the urine, but at the end of two hours the blood-sugar concentration will be at or below the fasting level. The fasting level always is within normal limits. The difficulty apparently is a "lag" in the rapidity with which the glucose disposing-mechanism of the body becomes active; once this mechanism is started it very quickly disposes of the excess glucose in the blood causing a rapid fall in the blood-sugar concentration.

Some students of this subject are depending for their diagnosis of the type of glycosuria more on the rapidity with which the blood-sugar concentration reaches the fasting level than upon the maximum blood-sugar concentration. Whether patients with this type of glycosuria eventually become diabetic will depend upon the observation of a large number of cases over a long time. Holst has stated, "that if a transition of a glycosuria

with a normal fasting blood-sugar into diabetes occurs at all it is at any rate a very rare phenomenon."

This type of periodic glycosuria is illustrated by the following case: D. R., a medical student, twenty-four years of age, applied for admission to the medical corps of the navy, and was rejected because sugar was found in his urine. Several fasting blood-sugar determinations were made at the University Hospital, and all fell well within the normal fasting level. He had none of the subjective symptoms of diabetes. It then was decided to determine his sugar tolerance by giving him 100 grams of glucose by mouth after fasting all night. The blood-sugar concentration was determined before and a half-hour, one hour, and two hours after the ingestion of the glucose. The following figures were obtained:

	Per cent.
Fasting blood-sugar concentration	0.101
Half-hour after glucose	0.193
One hour after glucose	0.111
Two hours after glucose	0.070

Sugar was discovered in the urine one hour after taking the glucose. This student was advised to lead a normal life, to ignore the presence of glucose in his urine, and to have his blood-sugar determined at regular intervals. The subsequent determinations of his fasting blood-sugar have revealed normal figures.

It would seem that there are no indications for treatment in these cases. They are advised, however, to subject themselves to periodic examinations to rule out the possibility of becoming diabetic. If there is a history of diabetes in the family it is advisable that they be cautioned against overindulgence in carbohydrates.

BIBLIOGRAPHY

1. Richards, A. N.: Kidney Function, Amer. Jour. Med. Sci., 1922, 163, 1.
2. Holst: Acta Med. Scandinav., 1925, 63, 47.
3. Jonas, L.: Renal Glycosuria, Clinics North America, 6, 1079, January, 1923.
4. Richardson, H. B., and Ladd, W. S.: The Utilization of Carbohydrate in a Case of Renal Glycosuria, Jour. Biol. Chem., 1925, 63, 681.

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THE HEART IN TUBERCULOSIS[1]

THERE are a number of infections apart from rheumatic fever and syphilis, such as diphtheria, influenza, and typhoid fever, also certain toxic states, such as hyperthyroidism, which damage the heart and disturb the circulation. This disturbance is due to impaired efficiency of the heart as distinguished from damaged valves or aorta.

That tuberculosis may also affect the heart is not always appreciated. This is probably because striking changes are seldom found at postmortem, and during the course of the disease the symptoms are often overshadowed by phenomena occurring in the lungs and by certain evidences of toxemia. There may be miliary tubercles in the myocardium following the acute disease or large caseous tubercles. Tuberculous endocarditis is also found, but, as in the myocardium, morbid findings in the valves are exceedingly rare. Tuberculous pericarditis is more common. The degenerative changes in the myocardium of tuberculous patients are not characteristic because they are found in other debilitating diseases. Until certain features of disease are understood more fully at postmortem it is necessary to consider them clinically.

The following cases are presented today because they suggest the harmful effect of tuberculosis upon the heart:

Case I.—E. H., an unmarried seamstress, aged fifty-one, entered the hospital November, 1925, complaining of cough, ex-

[1] From the Department for Diseases of the Chest, Jefferson Hospital.

pectoration, and shortness of breath. Her past history is irrelevant except for measles and whooping-cough in childhood and pleurisy with effusion in 1911, which lasted for six weeks and caused her to lose 8 pounds in weight. She returned to good health except for an occasional head cold and attacks of bronchitis during the winters and moderate shortness of breath on exertion for several years. Three months before entry she developed a cough with moderate expectoration. A tuberculous process was found in the right lung and tubercle bacilli were noted in the sputum. She had an afternoon temperature of 100° to 101° F. for seven weeks and a pulse varying between 90 and 100. After having been at rest for sixty-nine days, her symptoms subsided and she was permitted to take moderate exercise. Six days before entry swelling of the ankles, cyanosis, palpitation of the heart, and marked shortness of breath appeared. The afternoon temperatures were 99.4° F.

Physical examination showed an emaciated woman with moderate dyspnea, cyanosis, and edema of the lower extremities. The cardiac impulse was feeble, diffuse, and extended outside the nipple line. On auscultation the sounds were distant and irregular in every way, but no murmurs were heard. The rate was 150. The pulse rate was 90 and also grossly irregular. The examination of the lungs showed impaired resonance, roughened prolongation of the expiration, and a few coarse râles over both apices. The percussion note over the bases was impaired and there were numerous râles. The laboratory findings showed occasional hyaline and granular casts in the urine and tubercle bacilli in the sputum. In the roentgenologic study a small area of infiltration, fibrous changes, and cavity formation were noted in the apex of the right lung and scattered areas of fibrosis with a few calcified bodies in the left apex.

The circulatory symptoms failed to improve during the first two days in the hospital. She was given Karrell diet (800 c.c. of milk daily), 15 minims (1 c.c.) of tincture of digitalis every six hours for three days, and on the fourth day continued on house diet without medication. One week later a striking decrease of edema was noted with lessened cough and cyanosis. On the

tenth day the heart was found to be regular with a rate of 86, and the sounds were improved. She was entirely symptom free seven weeks after entry and was permitted moderate exercise. After this, however, the heart again became irregular with associated slight dyspnea and cyanosis. A Roentgen-ray examination showed what appeared to be an arrested tuberculosis, but on account of the cardiac condition the patient was returned to bed. On frequent examination of the heart the rate and rhythm were found to vary considerably. There were periods of several hours when the heart was regular, and then abruptly the heart would become grossly irregular with a marked pulse deficit. The longest period of irregularity noted was eighteen hours. An electrocardiographic study showed this to be transient auricular fibrillation. Within about seven days these attacks ceased, but the patient remained in bed until the fifteenth week after entry. She then resumed moderate exercise without recurrence of this phenomenon.

The progress of this patient emphasizes the importance of considering the response of the heart to effort as well as the response of the lungs to various activities. It is essential that the lungs should be examined regularly for evidence of active tuberculosis, but the heart examination should not be overlooked, especially during the first periods of exercise. A disturbance such as transient fibrillation should be regarded as possible evidence of injury to the myocardium. There is no reason to believe that tuberculosis has any definite etiologic relationship to the phenomenon which occurred in this patient, other than being a possible immediate precipitating cause. When attacks of transient auricular fibrillation occur, however, there is a reason to expect their reappearance. In treating such a condition, therefore, one should consider the heart as specifically as the tuberculosis. This is particularly important when there are marked alterations in the lungs, such as a fibrosis and retraction, which may interfere with the pulmonary circulation and be a serious burden to the heart. A history of previous circulatory failure, as was noted in this patient before entry to the hospital, should be a further reason for cautiously increasing exercise.

Case II.—R. C., a married housekeeper, aged thirty, entered the hospital November 18, 1925, complaining of a productive cough, bloodspitting, and palpitation with dyspnea on exertion. The past history is essentially negative, except that she has always been underweight and has never been considered a strong person. She has suffered frequently from bronchitis. Five years ago her first child was born and for about six months she was weakened and unable to do her housework. Three years later a second child was born and for several months she again noticed a marked loss of strength. In 1924 she was somewhat improved. Nine months before entry a productive cough, increased weakness, and progressive loss of weight occurred. She remained in bed for about five months with considerable improvement, but on returning to her household duties her symptoms became aggravated. Her fever was frequently above 100° F. and her pulse rate varied between 90 and 110. She rested infrequently. Ten days before entry she noticed slight swelling of the ankles. This followed a period of rapid heart rate with marked palpitation. Shortness of breath and increased cough with bloodspitting occurred two days before admission.

Physical examination showed a feeble cardiac impulse within the mammillary line. The cardiac area of dulness appeared within normal limits. The heart sounds were distant but regular. No murmurs were heard. The heart rate was 104. The lung examination showed limited expansion, impaired resonance, bronchial breathing between the clavicle and the fifth rib on the left side. Numerous râles were present. On the right side there were similar but less extensive signs. The sputum was positive for tubercle bacilli on three examinations. The urine was essentially negative except for a trace of albumen. The basal metabolism was normal. The Roentgen-ray examination showed slight infiltration and evidence of chronic tuberculosis over the areas corresponding to the physical signs.

The shortness of breath and palpitation disappeared after the third day, and there was less cough and expectoration after the second week, but the fever and the increased heart rate of between 100 and 110 continued for ten days. Fourteen weeks

after entry marked general improvement was noted, and she was permitted moderate exercise. On one occasion during effort she suddenly became very short of breath and cyanotic, and her heart rate was found to be 190 and regular. The heart sounds were distant and tic-tac in quality. Repeated attempts to end the attack by pressure on the right and left vagus nerves were unsuccessful, but the attack was ended abruptly after about twenty minutes when the patient's head was placed between the knees. There was no opportunity to confirm the diagnosis by electrocardiogram, but the regular heart beat of 190, the sudden onset, and the abrupt ending of the phenomenon seemed characteristic of paroxysmal tachycardia. She was returned to bed, but three other attacks occurred, one of which was followed by bloodspitting and lasted for more than four hours, although vagal and ocular pressure was applied frequently. The patient remained in bed for two months after the last attack. She has been on moderate exercise for three weeks without recurrence of the phenomenon.

The tachycardia which occurred in this patient was quite different from that seen ordinarily in tuberculosis. In each attack the onset was sudden and the ending abrupt. The precipitating cause for the attacks, aside from the possible influences of unaccustomed effort, is uncertain. There appeared to be no gastro-intestinal, emotional, or metabolic disturbances, and the pulmonary infection was apparently quiescent. That the phenomenon can be attributed to the effect of tuberculosis is doubtful; however, the prolonged illness may have influenced the myocardium and is sufficient reason to consider a relationship. Although the origin of the disturbance is uncertain, this patient seems to emphasize the importance of close observation of the heart during the first periods of exercise, following an active tuberculous infection. This is especially true if there is a history of previous circulatory failure. It is to be remembered that certain signs and symptoms, such as dyspnea, palpitation of the heart, exhaustion, sweating, pallor, and bloodspitting may occur in paroxysmal tachycardia. Many of these symptoms are commonly noted in tuberculosis, but their sudden onset and abrupt

termination should always suggest a disturbance of the circulation. In tuberculosis, certain complications influence unfavorably the course of the disease. It is important, therefore, that disorders of the heart beat, which in themselves may be serious, should be recognized and treated without delay.

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OBSTRUCTIVE JAUNDICE

THE liver has been the object of numerous contributions in recent years both from experimentalists and clinicians. The experimentalists have been stimulated to renewed efforts because of outstanding and somewhat revolutionary contributions by some of their number. Clinicians are ever on the alert to apply new interpretations to their findings when they appeal more to their judgment or add constructively to diagnostic or therapeutic skill. The late additions to our knowledge of liver physiology and pathology have probably surpassed those of any other vital organ. This has been largely made possible by the contributions of Archoff and his pupils, Van den Bergh, McNee, Whipple, Mann, Rich, Rosenthal, Rous and his co-workers, Lyon, and many others. Our interest in the mechanism of jaundice has been stirred up anew after a lethargy of years. It is the purpose of this clinic to discuss briefly the problems encountered in obstructive jaundice in the light of recent advances and new theories. The outstanding feature of jaundice is the deposit in the tissues of bile pigment which is visible to the eye. In obstructive jaundice the excretory duct apparatus of the liver is at fault and the biliary elements are absorbed and accumulate in the circulation and tissues. In order to properly understand this phenomena it is necessary to consider briefly the origin and physiology of the biliary constituents which are usually retained in the circulation in this condition, *i. e.*, bile acids, bile pigments, and cholesterol. Other biliary elements are probably concerned, but our knowledge of them is too meager for intelligent discussion.

BILE SALTS

The first of these, the bile acids, are usually present in the bile of most animals as the sodium salts of glycocholic and taurocholic acids. Cholic acid, a constituent of both salts, has often been considered a close kin of cholesterol. The work of Foster, Hooper, and Whipple[1] throws some doubt upon this relationship. They found that cholesterol fed alone or combined with taurin causes no change in the excretion of bile salts. The other portion of the radical is either glycin or taurin. The source of the latter is, in all probability, the cystin of the food. It is the cholic acid supply which appears to be the normal limiting factor which determines the bile acid level of excretion. As regards the site of formation of bile salts it may be said that the evidence, though incomplete, is all in favor of the hepatic epithelium. Foster, Hooper, and Whipple[2] observed that an Eck fistula liver which is functionally subnormal excretes much less bile salt than does a normal liver. In more recent work Smyth and Whipple[3] found that very small doses of chloroform by mouth may often reduce the content of bile salts in bile fistula almost to zero. The quantitative method for bile salts used in these experiments was described by Foster and Hooper.[4] An accurate clinical method for the quantitative determination of bile salts in the blood would add considerably to our knowledge of jaundice. We know of no such method at the present time.

CHOLESTEROL

A second constituent of the bile which has been given considerable attention and which is probably responsible for some of the manifestations in obstructive jaundice is cholesterol. This substance is widely distributed in the body and exists both free and in combination with fatty acids. Chemically it is an alcohol and not at all similar to the fats, although very similar to them physically. The origin of normal cell cholesterol is unknown. Stadleman[5] suggests the origin for cholesterol from the bile-duct epithelium and degenerating liver cells. Kosumoto,[6] from experiments on bile fistula dogs, concludes that a part at any

rate of the cholesterol of the bile arises from the débris of the normal destruction of red blood-cells.

Cholesterol feeding experiments to determine its effect on bile or blood cholesterol have yielded variable results. Stadleman[7] and Goodman[8] found no increase in bile cholesterol following cholesterol feeding. On the other hand, Frazer and Gardner[9] state that when cholesterol is given with the food to rabbits, some is absorbed and finds its way into the blood-stream as free cholesterol. This positive finding in regard to the effect of cholesterol feeding finds confirmation in the work of Fasiani,[10] D'Amato,[11] and Ludin.[12]

That the synthesis of cholesterol may take place in the animal body has convincing support from the work of Gamble and Blackfan[13] and Gardener and Fox[14] in humans, and that of Randles and Kundson[15] in their studies on white rats. The rôle and fate of cholesterol in the body is also not definitely known. From their experiments Fraser and Gardener[9] state that it increases the antihemolytic power of the blood-stream. Doree and Gardner[16] express the opinion that cholesterol should not be regarded as a waste product, having shown[17] that herbivorous animals do not excrete cholesterol or any recognizable derivative of that body in their feces, although their bile contains considerable quantities. A view has been advanced that much of the cholesterol excreted into the intestine is reabsorbed and again distributed to the body cells for further utilization.

BILE PIGMENT

Concerning the formation of bile pigment a very active controversy has existed almost since Vichow,[18] in 1847, discovered in old hemorrhages a pigment (hematoidin) which resembled bilirubin. The identity of these two pigments has been recently established by Rich and Bumstead,[19] and by Fischer H. of Munich.[20] Even earlier, in 1844, Müller[21] reported that he was unable to detect bile pigment in the blood or tissues of hepatectomized frogs which lived for four days. Moleschott[22] confirmed these findings, thus advancing evidence for the purely hepatic origin of bile pigment. Stadlemann[23] endorsed this by advanc-

ing the view that jaundice produced by hemolytic agents is essentially obstructive, based on the conclusion that increased blood destruction produced a thickened bile, which, in turn, obstructed the finer bile-ducts in the liver. Afannassiew[24] two years later (1883) from similar experiments came to the same conclusion.

With the above-mentioned work apparently negativing Virchow's contention, it remained for the experiments of Minkowski and Naunyn[25] in 1886 to firmly entrench the view that an "anhepatogenous icterus," a term proposed by Quincke[26] in 1884, did not exist. They removed the livers from hens, ducks, and geese, and found that the marked jaundice which regularly followed intravascular hemolysis in normal birds failed to make its appearance in these dehepatized animals. This led to quite a universal acceptance of the dictum, "without the liver, no jaundice."

It is illuminating to see upon what scanty evidence this view was maintained for nearly thirty years. McNee[27] in 1913 repeated the experiments of Minkowski and Naunyn, and while he was able to confirm their findings in the main, offered further evidence to show that the liver of birds contains the major portion of the system of cells which is now believed to be the site of bile-pigment formation. In the same year Whipple and Hooper's[28] work appeared. This first seriously attacked the purely hepatogenous view of jaundice. Their experiments and conclusions are so well known that it will be unnecessary to repeat them. Suffice it to say that the acceptance of their work threw the purely hepatogenous view of jaundice largely into the discard, where it remained for about ten years. The whole controversy was vigorously renewed by the work of Rich[29] and Makino,[30] who pointed out the fallacy in Whipple and Hooper's experiments, namely, that the liver and thoracic circulations were still in communication. McNee and Prusik[31] also repeated Whipple and Hooper's experiments, but were unable to confirm their findings. We thus find ourselves practically thrown back to 1886 to the work of Minkowski and Naunyn, it having been demonstrated apparently that Whipple and Hooper's work was inconclusive.

The next important contribution was that of Mann, Bollman, and Magath,[32] who removed the liver completely and at the same time maintained the circulation from the abdominal viscera and posterior extremities. They found that urine obtained from a hepatectomized animal a few hours after operation was bile tinged, and gave a positive reaction for bilirubin. From three to six hours after the removal of the liver the plasma assumed a yellow tinge. This color usually increased progressively until death, the reaction for bilirubin being positive.

Rich[33] believed that the time interval between the primary operation and the actual hepatectomy in Mann's dogs was possibly great enough to allow an extra hepatic compensatory mechanism for bile-pigment formation to function. In view of this he devised his complete evisceration operation in which the liver is removed without any previous interference with its functions and at the same time the entire musculoskeletal system is left within the circulation. In two of three dogs so operated upon bile pigment made its appearance in the plasma in two, (four and six and a half hours after evisceration) and in a fourth dog the addition of hemoglobin to the circulating blood was followed by the appearance of bilirubin in the plasma in a time much shorter and in amount much greater than in the previous experiment. He thus confirmed the conclusion of Mann, et al, that bile pigment can be formed in an animal from which the liver and all the other abdominal viscera have been removed if the circulation be maintained through the entire musculoskeletal system. Rich further believes that there is undoubtedly, outside the liver, a mechanism, which, if it is not continually active in bile-pigment production under normal conditions, can certainly assume that function upon immediate notice.

The question now arose whether the yellow pigment which developed in these experimental animals was really bile pigment. The argument was advanced that the chemical tests for bilirubin cannot be considered specific. To answer this contention Mann, Magath, and Sheard[34] resorted to the physiochemic method of identification of the pigment. They compared the curve of light transmission of the yellow pigment appearing in

the blood of a totally dehepatized animal, of an animal totally dehepatized without preliminary operation, of an animal with its common bile-duct obstructed and gall-bladder excised, and with the bilirubin found in the gall-bladder of the dehepatized animals at the time of removal of the liver. They found that a yellow pigment appeared in the plasma of each of these animals within three to six hours after operation. As determined by the spectrophotometer, the curves of light transmission of the pigment in the plasma of these animals was identical in nature to that obtained with the gall-bladder bile at time of operation.

Aside from the above direct experimental evidence that extrahepatic formation of bile pigment is possible, other evidence favoring this view had accumulated for some time. Thus Tarchanoff[35] found bilirubin in the urine of bile fistula dogs after hemoglobin injections. Froin, in examining 178 hemorrhagic fluids from the peritoneum, pleura, and cerebrospinal fluid, found bilirubin present in 53 cases. Whipple and Hooper[36] were able to demonstrate the formation of considerable quantities of bilirubin from hemoglobin injected into the peritoneal or pleural cavities of dogs. Van den Bergh[37] records the findings in a case of sarcoma of the lung with large hemorrhagic pleural exudate. The bilirubin content of the exudate was 1/30,000, while the peripheral blood showed only 1/360,000. Rich and Bumstead[19] report a similar experience with the bilirubin content of an omental cyst in a child. Jones and Jones[38] found bile pigment in the blood of a patient's arm constricted with a tourniquet, following an attack of paroxysmal hemoglobinuria.

As regards the distribution of the cells concerned in the formation of bile pigment, the discussion hinges largely around the reticulo-endothelial system developed by Aschoff[39] and his pupils. A discussion of this system would be beyond the province of this paper. While it is true that we have no clinical diseases which would appear at this time to be due to the disordered function of the reticulo-endothelial cells, there is experimental evidence from Lepehne that the blocking of this system by means of innocuous silver compounds may hinder the development of experimental hemolytic icterus. That the explanation for the

results obtained by Minkowski and Naunyn in their experiments on geese depended on the removal of the major portion of this system was shown by McNee.[27]

Evidence that the spleen can form bilirubin has been advanced by showing a greater content of bilirubin in the blood of the splenic vein as compared to peripheral blood. Such data has been recorded by Van den Bergh and Snapper,[40] C. H. Andrewes,[41] Kaznelson,[42] and Rich and Rienhoff,[43] while Charrin and Moussu[44] and Goto, K.[45] showed that the removal of the spleen may cut the output of bile pigment in half. The clinical significance of bilirubin estimations in the blood, urine, bile, and feces will be considered later.

UROBILIN

Although this pigment is a derivative of bilirubin, its significance is such as to necessitate a separate consideration of it, when jaundice of any variety is under discussion. Urobilinuria has come to occupy a place of importance in the study of all cases in which liver dysfunction, biliary tract disease, and blood destruction are under suspicion. Urobilin was discovered by Jaffe[46] in 1869, who noted an absorption band spectroscopically in a specimen of urine. He also discovered its presence in normal bile. Its presence in normal stools was first observed by Masius and Vanlair[47] in 1871. Since that time its presence in the urine has been thought by a number of observers to be indicative of liver dysfunction or blood destruction. It has very frequently been found in cases of pernicious anemia, hemolytic jaundice, and cirrhosis of the liver. Elman and McMaster[48] have recently summarized our knowledge of the chemical nature of urobilin by saying "that it is a reddish-brown pigment, derived from bilirubin by reduction in the body, or from urobilinogen by simple oxidation in vitro. Urobilinogen, the usual reduction product of bilirubin, is a normal constituent of bile and feces, and at times of urine in traces. As the chromogen of urobilin it is spontaneously oxidized to it in the air." The previous methods for the determination of urobilinogen and urobilin depend upon (1) the spectroscopic absorption bands, (2) fluorescence in the pres-

ence of saturated alcoholic solution of zinc acetate,[49] and (3) the appearance of a red color in the presence of Ehrlich's aldehyd reagent (2 gm. of paradimethylamidobenzaldehyd in 100 c.c. of 20 per cent. HCl). The method used by Elman and McMaster is one of comparative fluorescence. A certain amount of acriflavin is dissolved in water and the zinc acetate filtrate from the urobilin containing solution is diluted till it matches this color. The standard itself is calibrated against the fluorescence of a standard solution of urobilin.[48] The urobilinogen is disregarded in their method, "since it is easily oxidized to the more readily recognizable urobilin." They believe that the method might be adopted for clinical purposes. The method would seem to be the most accurate yet devised, but it is probably a little complicated for routine use. A much more simple quantitative method has recently been advanced by Wallace and Diamond.[50] It is based upon Ehrlich's aldehyd reaction, a series of dilutions being made until no further reaction takes place. This is a test for urobilinogen, which they perform on freshly voided specimens.

Elman and McMaster have shown that normally the presence of urobilin in the bile and feces of dogs depends upon the presence of bilirubin in the intestine, *i. e.*, when the intestine is deprived of bile experimentally urobilin will disappear from the body. The feeding of bile to such dogs whose intestinal tracts have been deprived of it by operation causes the reappearance of bile in the feces and bile. Experimentally the amount of urobilin in hepatic bile and feces is proportionate to the quantity of bile in the intestine. Friedrich Müller,[51] Fromholdt and Nersessoff,[52] and Fischer and Meyer-Betz[53] have taken patients with complete obstructive jaundice without a trace of urobilin in the urine, whom they fed urobilin free bile and observed the appearance of urobilin in the feces and urine.

McMaster and Elman[54,55] have offered direct proof of the absorption of bile pigments from the intestinal tract. Their experiments seem to conclusively prove that the damaged liver does not manufacture urobilin unless it be infected. Urobilin is never found after liver injury unless bile is present in the intestine. The only extra-intestinal source of urobilin is in the

infected biliary tract, where certain organisms cause it to be produced from bilirubin. Wallace and Diamond[50] have similarly concluded concerning the rôle of the liver and intestine in urobilin formation. McMaster and Elman[56] have also explained the appearance of urobilinuria in increased blood destruction. The liberation of large amounts of hemoglobin causes an increased output of bilirubin in the bile which insures an increase in the amount of urobilin formed in the bowel. The quantity of urobilin which is absorbed is too great for the liver to handle, and part escapes into the general circulation to be eliminated by the kidneys. Urobilinuria does not occur in association with increased blood destruction in the absence of bile from the intestinal tract. This explains the existence of urobilinuria in the acute stages of pernicious anemia and in some acute infectious diseases. That liver damage may also play a part cannot be denied, as it would reduce the amount of urobilin which the liver can handle.

These observers have shown that interference with function of only one-third of the liver (by duct obstruction) will cause urobilinuria. Bilirubinemia only occurs when obstruction or liver damage is considerable.[57] The presence of urobilin in the urine is, therefore, a valuable finding because it makes manifest biliary disturbances of a mild degree. Urobilinuria is always absent in complete obstructive jaundice, unless (1) there is infection of the biliary tract or (2) very rarely, if the jaundice has existed for a long time, bilirubin may be excreted through the intestinal mucosa as a result of intense icterus of the cells, and traces of urobilin may be formed. We must be cognizant of the fact that a great many cases of obstructive jaundice are not complete, *i. e.*, some bile escapes into the intestine; urobilin is very often found in the urine in such cases. Even though the amount of urobilin formed is small, the damaged liver in such cases interferes with its hepatic excretion. Urobilinuria is frequently present during the early stages and during convalescence from acute catarrhal jaundice, but is rarely found during the height of the jaundice. We cannot agree with the construction placed upon the significance of urobilinuria in catarrhal jaundice as

compared with obstruction due to outside pressure by Wallace and Diamond. They claim it is a constant finding in catarrhal jaundice and that it is never present in obstructive jaundice. We are still old-fashioned enough to believe in the old Virchow conception of catarrhal jaundice, that it is primarily an obstruction of the common duct. Clinically, in our experience the obstruction in severe cases is just as complete in this condition as in any other lesion causing obstruction. At the height of the jaundice urobilin is practically never present. During the period of recrudescence it is almost invariably found. The same applies to obstructive jaundice of any other cause, carcinoma of the head of the pancreas included; if the block is complete, urobilin is absent (barring infection); if it is incomplete, it is apt to be present. After a very extensive experience with duodenal tube drainage in cases of jaundice we feel justified in stating that in most cases of severe catarrhal jaundice we find a minimum of bile in the duodenum, often practically none at the first intubation. The type of bile flow in these cases is totally different from that which occurs in hepatitis, *e. g.*, arsphenamin jaundice. In these cases bile flow is usually appreciable in spite of deep icterus. Urobilinuria in portal cirrhosis occurs in the absence of jaundice, excessive blood destruction, or obstruction. The escape of portal blood directly into the general circulation by way of various anastomotic channels can easily account for it according to McMaster and Elman.

Summing up, the site of manufacture of urobilin is the intestinal tract, from bilirubin (only exception being the biliary tract when it is infected). Its appearance in the urine depends upon the degree of activity of the liver parenchyma. Clinically, it is significant of liver damage or increased blood destruction.

THE VAN DEN BERGH REACTION

The contribution of Van den Bergh and Snapper[58] in 1913, followed by Van den Bergh's excellent monograph,[37] introduced a chemical method in the study of jaundice which has in recent years done more than any other single procedure to stimulate investigation of this subject. To McNee[59] we are indebted for

introducing this test to the English-speaking world, as his article was the first to appear in the English language. McNee advances the theory that the polygonal cells of the liver are not essentially concerned with the manufacture of bile pigment, but have chiefly to do with its transference from the vascular capillaries into the bile capillaries. The theory is advanced that in passing through the polygonal cells the bile pigment is modified in some way. It is the cells of the reticulo-endothelial system which are assumed to be primarily concerned with the breaking down of hemoglobin and the elaboration of bile pigment. On the basis of this hypothesis, McNee considers the circumstances under which icterus might develop:

"(1) Where bile pigment, formed in the cells of the reticulo-endothelial system, passes through the polygonal cells normally to reach the bile capillaries, but is obstructed there and finally reabsorbed into the blood.

"(2) Where, owing to damage to the polygonal cells of the liver, the bile pigment carried to them by the endothelial cells is unable to enter them. The bilirubin would, therefore, pass directly along the hepatic venous radicles into the general circulation. On the other hand, part of the bilirubin might pass through and part be unable to do so.

"(3) Where, in excessive blood destruction, too much bilirubin is formed in the reticulo-endothelial system for the polygonal cells to deal with. Some pigment might pass normally into the bile capillaries and color the feces, while the excess might pass straight through and bring about jaundice.

"(4) Where, in addition to damage and disordered function of the polygonal cells, there is also obstruction in the bile-ducts, for example, cholangitis. Some pigment might pass directly through the hepatic vein into the circulation and some through the polygonal cells to be afterward reabsorbed on account of obstruction."

Clinically McNee classifies jaundice as:

(1) Obstructive hepatic.

(2) Toxic and infective hepatic.

(3) Hemolytic.

The qualitative Van den Bergh reaction (for technic and interpretation, see McNee[60]) supposedly was intended as an aid in differentiating these types clinically. In the purely obstructive cases according to this theory the bile pigment is formed normally by the Kupffer cells let us say, passes through the polygonal cells of the liver, is obstructed somewhere in the duct system, and is reabsorbed into the circulation. This type of

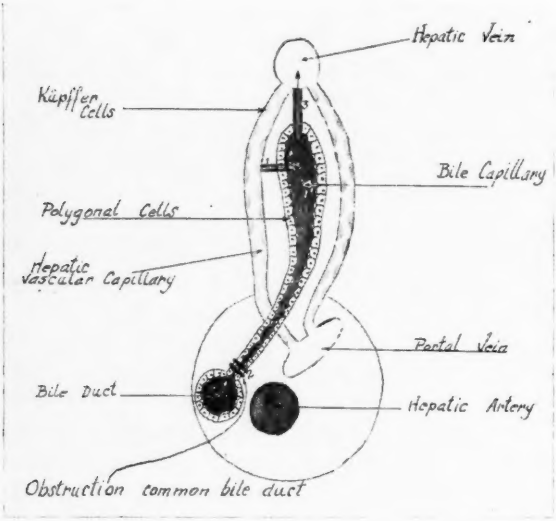

Fig. 40.—Obstructive jaundice. Direct reaction. Bile pigment passes from Kupffer cell 1 through polygonal cell of liver. Obstruction of common bile-duct at 2. Bile absorbed into circulation at 3. (After McNee's drawing.)

serum should give a direct immediate qualitative reaction according to the Van den Bergh classification (Fig. 40). With fully developed obstructive jaundice we have found this to be true. On the other hand, it has been our experience, as well as that of others (*e. g.*, Bloom[61]), that in the early stages of obstruction the qualitative reaction may be direct, delayed direct, indirect, or biphasic. This leads one strongly to suspect whether the concentration of bile pigment in the serum is not a factor

in the type of qualitative reaction obtained. We have obtained variable qualitative reactions with various dilutions of bile obtained from the gall-bladder of a rabbit in which the duct had been tied off for several days. With the concentrated bile a reddish-brown color was obtained by the direct method, and the typical color of the direct immediate reaction was only obtained after considerable dilution of the bile before carrying out the

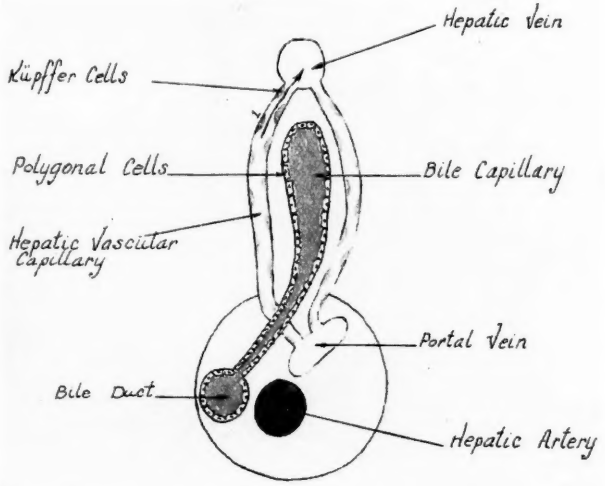

Fig. 41.—Hemolytic jaundice. Indirect reaction. Blood destruction so fast that polygonal cell of liver cannot transmit all of pigment which is formed. Consequently, some pigment passes directly into circulation 1 without passing through polygonal cell. (After McNee's drawing.)

test. In hemolytic jaundice the excessive hemolysis leads supposedly to the formation of bilirubin over and above the amount which the polygonal cells can handle and excrete into the bile. The result is that the excess enters the circulation without passing through the liver cells. This type of bilirubin gives the indirect or, at the most, a delayed direct reaction (Fig. 41). Most observers agree that this type of reaction is the rule in hemolytic icterus. Our experience has usually been in accord with these findings.

The type of case in which the most variable reactions have been reported, and in which group Feigl and Querner[62] observed the biphasic reaction, is the toxic and infective group (Fig. 42). In this group the cause of the jaundice (obstructive or non-obstructive) is most difficult to determine. Unfortunately, in these cases the qualitative Van den Bergh is so variable as to

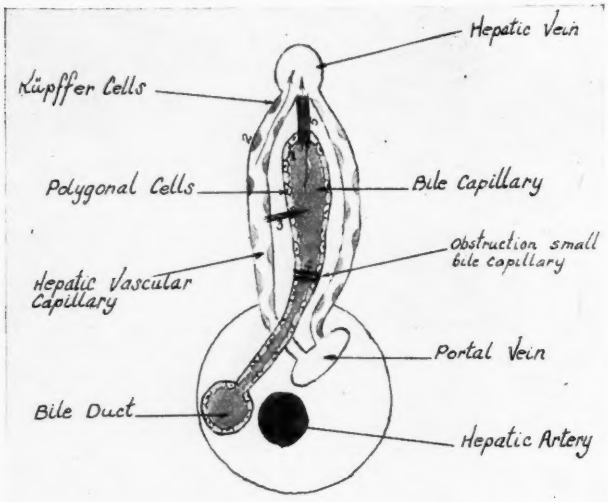

Fig. 42.—Toxic infectious jaundice. Biphasic reactions. Polygonal cell damage 1 sufficiently great to prevent all pigment from passing through polygonal cell, consequently some pigment passes directly into the circulation. 2. The pigment which passes through the polygonal cell 3 meets with obstruction in small bile capillaries at 4, and is absorbed into circulation at 5. (After McNee's drawing.)

be of no value whatever. This last statement should be made with reservation. It is quite possible when we understand the pathology of this complex group more thoroughly, and when the Van den Bergh qualitative reaction has been studied more extensively in experimental jaundice, many of these apparently paradoxic reactions will be adequately explained. The classification of jaundice based on this theory is certainly an attractive

one, and helps one to visualize what is going on probably better than any grouping previously offered. That there is a difference in the bilirubin in cases of obstructive and hemolytic jaundice seems plausible. Be it some alteration in the chemical constitution of the bilirubin molecule or a union with some albuminous substance in the indirect bilirubin as suggested by Van den Bergh,[37] or a lipoid linkage as suggested by Feigl and Querner,[62] or purely some physical difference as intimated by Andrewes,[63] remains to be proved. The fact remains that very definite differences in the two types of bilirubin were noted by Van den Bergh, and these differences have been multiplied by later investigators. For an excellent review of this phase of the subject, see article by Andrews.[64]

When we consider the quantitative reaction, we have a method for following the degree of jaundice in a patient which is certainly not surpassed and probably not equaled by any other. This holds true particularly if the technic is carried out as modified by Thannhauser and Andresen.[84] The icterus index which has found many advocates recently, while simpler to carry out, is probably not as accurate because of the possibility of erroneous readings due either to other pigments or slight hemolysis in the serum. Incidently the use of the cobalt sulphate standard, as described by McNee and Keefer,[65] will doubtlessly be a great help both in the ease and accuracy with which the quantitative reaction can be carried out. The normal quantity of bilirubin in the serum as recorded in Van den Bergh units is 0.2 to 0.5 unit. One unit has been arbitrarily chosen to represent one part of bilirubin in 200,000 parts of serum. The normal variations then are from one part per 1,000,000 to one part per 400,000.

The quantitative Van den Bergh is of definite value in following the course of a case of clinical jaundice, for the degree of skin coloring is no criterion of the actual amount of blood bilirubin. It has also established the fact that there are many conditions in which jaundice is not apparent, but an actual hyperbilirubinemia exists. This condition is spoken of as latent jaundice, *i. e.*, hyperbilirubinemia without pigment deposit or

bile in the urine. The kidney threshold for bilirubin in obstructive jaundice is about 4 units. At least that quantity of bilirubin will be present in the blood before bile appears in the urine. Variations in the kidney threshold occur.[67, 68] The kidney threshold for bilirubin in hemolytic icterus is very high, as it rarely appears in the urine in this type of jaundice. Latent icterus is frequently present in pernicious anemia and other hemolytic processes. It is claimed that the blood bilirubin estimation is helpful in differentiating primary from secondary anemia, as in cases of carcinoma (Andrewes,[67] Van den Bergh[68]). By its use a latent icterus has also been demonstrated in cases of cirrhosis and in the blood of the newborn. This determination has also been found useful in following patients under treatment with arsenicals. When the increase in blood bilirubin during treatment is heeded and the arsenicals stopped, many cases of arsenic jaundice will probably be avoided.

CLINICAL PHENOMENA IN OBSTRUCTIVE JAUNDICE

The signs, subjective and objective, which have been attributed to excessive quantities of bile in the blood may be classified as follows:

1. Cardiac: (*a*) Bradycardia, (*b*) irregularity of cardiac action, (*c*) lowered blood-pressure.
2. Skin: (*a*) Itching, (*b*) petechia, (*c*) xanthomata.
3. Nervous: (*a*) Depression, (*b*) coma, (*c*) paralysis.
4. Blood: (*a*) Tendency to spontaneous hemorrhage, (*b*) increased coagulation time of the blood, (*c*) decreased fragility of erythrocytes.
5. Bone changes: (*a*) Osteoporosis.
6. Urinary changes.
7. Stool changes.

1. **Cardiac.**—While most of these findings are usually attributed to the action of the bile salts, King and Stewart[69] state that the amount of pigment in a lethal dose of whole bile will cause death, but the bile salts present in the same quantity of bile will not cause recognizable effects. Fromholdt and Nersessoff[70]

state that the intravenous injection of 0.1 gm. of pure bilirubin will cause a fatal issue in rabbits. While it is not definitely established where the toxic action on the heart takes place, *i. e.*, vagus, intracardiac ganglia, or heart muscle, it has been shown that in some cases of icterus the administration of atropin stops the bradycardia. This suggests that these changes may be dependent on vagus irritation. King, Bigelow, and Pearce[71] ascribe most of the effects of bile on the heart to the bile pigments, perhaps through the extraction of calcium.

2. **Skin.**—The itching is generally believed to be due directly to the deposition of the bile salts in the skin. The xanthomata are probably deposits of cholesterol esters as a sequel of protracted hypercholesterolemia, which deposits lead to proliferative and phagocytic reactions in the fixed tissues.[72]

3. **Nervous.**—The nervous phenomena are also generally attributed to the action of bile salts, though some of these manifestations have been linked with the decreased available calcium in jaundice.

4. **Blood.**—The tendency to spontaneous hemorrhage seen particularly in jaundice of long standing and of which the petechia above noted are probably part, has been attributed by Morawitz and Bierick[73] to injury of the capillary endothelium by the bile salts. They have also investigated the delay in the coagulation time of the blood and found that the bile acids were not at fault, because even in the most severe cases the blood did not contain sufficient cholates to account for the delay. Others, however, have credited the bile salts with causing this delay, supposedly by interfering in the conversion of fibrinogen to fibrin. Haessler and Stebbins,[74] Koechig,[75] Bowler and Walters,[76] and Lee and Vincent[77] believe that it is probably due to the binding of the plasma calcium by the bile pigments, rendering the former unavailable for fibrin formation.

5. **Bone Changes.**—The osteoporosis seen in some cases of chronic icterus is probably also due to the decrease in available calcium.

6. **Urinary Changes.**—The change in color of the urine is due, of course, to elimination of bile pigments in the urine.

7. **Stool Changes.**—The clay color of the stool is due not only to the absence of bile, but, in addition, the large amount of total fat must be considered as the result of incomplete fat absorption due to the absence of bile in the duodenum.

BIBLIOGRAPHY

1. Jour. Biol. Chem., 1919, 38, 421.
2. Jour. Biol. Chem., 1919, 38, 393.
3. Jour. Biol. Chem., 1924, 59, 623.
4. Jour. Biol. Chem., 1919, 38, 355.
5. Der Ikterus und seine verschiedene Forman, Stuttgart, 1891.
6. Biochem. Zeit., 1908, 13, 354.
7. Zeitschr. f. Biol., 1896, 34, I.
8. Hofmeister's Beitr, 1907, 9, 91.
9. Proc. Roy. Soc., 1909, B. 81, 230.
10. Arch. Ital. de Biol., 1915, lvxi, 229.
11. Biochem. Zeitschr., 1915, lxix, 217.
12. Jour. Biol. Chem., 1916, 27, 257.
13. Jour. Biol. Chem., 1920, 42, 401.
14. Proc. Roy. Soc., 1921, xcii, 358.
15. Science, 1924, 60, 530.
16. Proc. Roy. Soc., 1908, Biochem., 81, 110.
17. Proc. Roy. Soc., 1908, Biochem., 80, 12.
18. Virchow's Arch., 1847, 1, 379.
19. Bull. Johns Hopkins Hospital, 1925, xxxvi, No. 4.
20. Quoted by H. Van den Bergh, Brit. Med. Jour., September 20, 1924, p. 498.
21. Handbuch der Physiologie des Menschen für Vorlesungen, 4 aufl., 1844.
22. Arch. f. Physiol., Heilk., 1852, xl, 479.
23. Arch. f. exper. Path. u. Pharmakol., Leipzig, 1881, Bd. xlv, ss., 231 and 422. Also Der Icterus und seine versehiedene Formen, Stuttgart, 1891.
24. Ztschr. f. Klin. Med., Berlin, 1883, vi, 281–331.
25. Arch. exper. Path. u. Pharm., 1886, xxi, 1.
26. Virchow's Arch., 1884, Bd. xc, U. S., 125.
27. Jour. Path. and Bact., 1913, xviii, 325.
28. Jour. Exp. Med., 1913, xvii, 593, 612.
29. Bull. Johns Hopkins Hospital., 1923, xxxiv, 321.
30. Ziegler's Beiträge, 1920, lxxii, 808.
31. Jour of Path. and Bact., 1924, xxvii, 9.
32. Amer. Jour. of Physiol., 1924, 69, No. 2.
33. Bull. Johns Hopkins Hospital, 1925, xxxvi, No. 4.
34. American Jour. of Physiol., September, 1925.
35. Pflüger's Arch., 1874, ix, 53, 329.
36. Jour. Exp. Med., 1916, xxiii, 139.
37. Der. Gallenfarbstofl im Blute, Leiden, 1918.
38. Arch. Int. Med., 1922, 129, 669.

39. Lectures on Pathology, 1924, Paul B. Hoeber, publisher, pp. 1 and 233.
40. Berl. klin. Wchnschr., 1915, lii, 1081.
41. Quart. Jour. Med., 1924, 69, 29.
42. Wien. Arch. f. inn. Med., 1920, 1, 563.
43. Bull. Johns Hopkins Hospital, 1925, No. 6.
44. Compt. rend. Acad. d. Sci., 1905, 140, 1118.
45. Jour. Exper. Med., 1917, 26, 795.
46. Virchow's Arch. Path. Anat., 1869, xlvii, 405.
47. Centr. Med. Wissensch., 1871, ix, 369.
48. Jour. Exper. Med., April 1,
49. Deutsch. Med. Woch., 1903, xxix, 561.
50. Arch. Int. Med., vol. 35, No. 6.
51. Verhandl. Congr. Inn. Med., 1892, xi, 118.
52. Z. exp. Path. u. Pharmakol., 1912, xi, 400.
53. Münch. Med. Woch., 1912, lix, 799.
54. Jour. Exp. Med., vol. xli, No. 6, pp. 719–738, June 1, 1925.
55. Jour. Exper. Med., July 1, 1925, vol. xlii, No. 1, pp. 99–122.
56. Jour. Exp. Med., November 1, 1925, vol. xlii, No. 5, pp. 619–640.
57. Jour. Exper. Med., June 1, 1921, vol. xxxiii, No. 6, pp. 731–750.
58. Deut. Arch. f. klin. Med., 1913, cx, 540.
59. Brit. Med. Jour., 1922, 1, 716.
60. Quat. Jour. Med., 1922–23.
61. Bull. Johns Hopkins Hospital, 1923, xxxiv, 316.
62. Ztsch. f. d. ges. exp. Med., 1919, 9, 153.
63. Brit. Jour. Exp. Path., 1924, 5, 213.
64. Deut. Arch. f. klin. Med., 1921, 137, 179.
65. Brit. Med. Jour., 1925, 2, 52.
66. Quat. Jour. Med., 1924, 18, 19.
67. Brit. Med. Jour., 1924, 2, 498.
68. Cited by Andrewes (9).
69. Jour. Exp. Med., 1909, 11, 673.
70. Biochem. Zeit., 1921, 125, 153.
71. Jour. Exper. Med., 1912, 14, 159.
72. Wells' Chemical Pathology, Saunders, 1925.
73. Arch. Exp. Path., 1907, 56, 115.
74. Jour. Exp. Med., 1919, 29, 445.
75. Jour. Lab. Clin. Med., 1924, 9, 679.
76. Ann. Surg., 1924, 180, 545.
77. Arch. Int. Med., 1915, 16, 59.

ILLUSTRATIVE CASES

Case I.—M. M., a colored widow, aged forty-nine, was admitted on September 4, 1925. Family history was irrelevant.

Past Medical History.—No typhoid. Urticaria ten years ago. Appendectomy fourteen years ago. No miscarriages. Menopause two years ago. Attacks of slight indigestion at infrequent intervals for years.

History of Present Illness.—Onset two weeks ago with epigastric fulness and belching. Consulted physician, who noticed icterus (slight) at that time. The jaundice has progressively increased. Bowels constipated since onset and have been very light in color. Urine has been wine colored for past week. States she has lost 10 pounds in two weeks. Diet has been liquid during that time. Laxatives have been used daily. Breath is disagreeable, and there is a bad taste in the mouth. No itching.

Physical Examination.—Many carious teeth. Pyorrhea. Many missing. Well nourished. Intense icterus present, as observed in conjunctiva and mucous membrane of mouth. Both lobes of liver palpable, right 1 inch below costal margin in midclavicular line. Blood-pressure, 180/105. Temperature, 99° F. Pulse, 80. Respirations, 20. Spleen not enlarged.

Patient obviously suffering from obstructive jaundice. Tentatively most likely cause was gall-stone disease or carcinoma of head of pancreas. These two conditions are given preference because they are most common causes of obstructive jaundice in a patient of her age. The jaundice is practically painless, generally considered to be a point against the diagnosis of gall-stones. The well-nourished state of the patient and inability to feel a mass might be said to be against the diagnosis of cancer of the pancreas. They are points of minor import, however. Several other possibilities were considered, *i. e.*, catarrhal jaundice, luetic hepatitis, carcinoma obstructing one of the main biliary excretory ducts. The first of these we diagnose only by exclusion in a patient in middle or late life. The absence of pain and the apparently excellent nutrition of the patient are in favor of that diagnosis however. We have seen several cases of gall-stone obstruction without pain and the absence of pre-

vious history of indigestion. It will be recalled that this patient admitted the existence of previous slight attacks of indigestion. Luetic hepatitis must be considered in a patient of this race. This condition rarely causes jaundice. We have not encountered such a case which has been confirmed by pathologic section. Of course, malignancy involving the liver or common duct must be considered. Clinically it does not seem likely. We will see what help can be derived from the laboratory examinations. Red blood-cells, 4,960,000. White blood-cells, 9620. Hemoglobin, 85 per cent. Differential normal. Van den Bergh direct immediate reaction, 40 units. Wassermann negative; Kahn negative. Coagulation time eleven minutes.

Blood-sugar 90 mg. per 100 c.c.; creatinin, 1.7 mg.; urea, 9 mg; uric acid, 5 mg.; cholesterol, 182 mg.; calcium, 11 mg. The low blood-urea and slight increase in cholesterol are the only things of note in the blood chemistry.

Sugar tolerance test: Fasting 90 mg. per 100 c.c.; thirty minutes, 150 mg.; one hour, 133 mg.; two hours, 85 mg. Tests for bile salts and pigment in urine positive.

Fractional gastric analysis: Low normal secretion. Emptying time slightly delayed. No gross occult blood or bile.

Stool: Very light color. Macroscopically negative, except for food. Neutral fat, fatty acid, muscle-fiber, and starch present. Occult blood negative.

Bile drainage was attempted on September 5th and 8th. The tube failed to pass through the pylorus on both occasions.

x-Ray of stomach and duodenum negative. Both freely movable. No filling defects. Emptying normal.

The immediate direct Van den Bergh, with very high bilirubin content of the serum, the moderately high-blood cholesterol, bile in the urine, almost complete absence of bile in the stool, all indicate the existence of obstructive jaundice. The comparatively normal erythrocyte count, the sugar tolerance, normal gastric acidity, absence of blood in the stool, sugar in urine, and negative *x*-ray findings are all against malignancy. The blood Wassermann and Kahn negative the likelihood of syphilis. The most probable diagnosis is gall-stone disease or

simple catarrhal jaundice. Our skepticism of catarrhal jaundice in middle life caused us to lean toward gall-stone disease. There are two other examinations which should prove of great value, *i. e.*, bile drainage and cholecystographic study. The first has been performed twice without success. It is of sufficient importance to warrant perseverance. We tried a third time, tying a small lead-shot to the metal tube tip with a silk thread about 8 inches long on September 12th. A successful drainage was obtained at this time. However, only 30 c.c. of brick-brown bile was obtained after the first stimulation with magnesium sulphate, which contained considerable flocculent material consisting of strands of mucus, pus, and phagocytic cells which so often are found in duodenitis.

A second stimulation of magnesium sulphate was applied to the duodenum and caused a return of 40 c.c. of dark brown bile, which microscopically was found to be swarming with motile flagellates, Giardia intestinalis, and bile-stained columnar cells. The third stimulation brought forth 50 c.c. of brown bile showing a similar microscopic picture. The failure to find cholesterin crystals and pigment in the bile, which we have so often found in the bile of gall-stone cases, together with the duodenal type of exudate and the numerous lamblia, caused us to lean toward a diagnosis of catarrhal jaundice. Previous to this we knew of no case of obstructive jaundice associated with giardiasis. Although we firmly believe these flagellates are often responsible for duodenitis, we hesitate to say that they are the cause of jaundice in this case.

A second Van den Bergh on September 10th showed 38 units of bilirubin, with an immediate direct reaction. The jaundice appeared more intense on the 10th in spite of the slight reduction in the bilirubin content of the serum. Patient developed small petechiæ at this time, which was the day following her gastro-intestinal *x*-ray.

Two days after the bile drainage patient felt better for the first time. No discernible decrease of icterus. On the 15th the Van den Bergh was immediate direct with 28 units, an appreciable decrease. It is not unfair to assume that drainage was

responsible for the marked decrease in blood bilirubin. This case emphasizes the importance of following the progress of the jaundiced patient with the blood bilirubin determinations rather than dependence upon clinical icterus. Patient was drained again on the 15th, with a similar result to that of the 12th. The Van den Bergh on the 18th showed a still greater drop to 10.5 units, the qualitative was biphasic. A third drainage was done on the 19th, 100 c.c. of bile being recovered. An enormous amount of flocculent material present contained pus, mucus, and low columnar cells, lightly bile stained, but over one-quarter of the flocculent material was made up of giardia.

The fourth Van den Bergh reaction on the 22d was biphasic with 4.2 units. Bile drainage on this date caused a recovery of 250 c.c. of bile, a very copious amount indicating an open duct. Some fine golden-yellow pigment was present for the first time. No giardia. Patient feeling fine. Clinical icterus decreased for first time, although the quantitative Van den Bergh took very substantial drop eight days previous (15th).

The finding of golden-yellow bilirubin pigment continued the uncertainty as to presence of stones. We performed an oral cholecystographic examination at this time. The result was not satisfactory. A definite small quarter-sized shadow was present, looking not unlike a collection of stones in the gall-bladder on a level with the third lumbar vertebræ. Almost continuous with this shadow was a shadow of dye in the bowel. It was not present on later films. Several days later an intravenous injection of tetraiodo dye was given, and a faint shadow was seen at the twelfth rib, undoubtedly gall-bladder. This was far removed from the shadow obtained after the oral administration of the dye, and illustrates the increased accuracy of the venous method. We hesitate to diagnose disease of the gall-bladder on finding a faint shadow because of lack of experience with this method on recently jaundiced people. There is nothing upon which to definitely base a diagnosis of gall-stones.

The Van den Bergh reaction on September 26th was biphasic, 2.1 units. The patient was discharged from the hospital on October 1st feeling well, with very little tissue icterus.

Weekly drainages for treatment were instituted from date of discharge until November 10th. An intravenous injection of 0.9 gm. of neo-arsphenamin was administered on November 3d for eradication of the giardia.

On October 13th the Van den Bergh was 2.6 units, delayed direct.

On November 3d it was 1.2 units, biphasic.

The Rosenthal liver function test (tetrachlor) on October 13th showed moderate dysfunction, *i. e.*, 9 per cent. in fifteen minutes, 5 per cent. in one hour, and 2 per cent. in two hours.

This case illustrates the inadvisability of operating upon a case of obstructive jaundice until every diagnostic aid has been utilized to eliminate non-surgical jaundice. Although we cannot definitely rule out gall-stones even now, their presence is very unlikely. We have always considered the finding of bilirubin calcium pigment crystals in the bile a point in favor of the presence of gall-stones. The very late and transitory appearance of this element suggests that it may only be an indication of long-standing stasis in the bile channels. After a few days of treatment we felt assured of a termination of the obstruction because of the reduction in blood bilirubin and the appearance of bile in the intestinal tract. It would have been folly to subject this patient to surgery even were we sure stones were present until the jaundice had disappeared. Whether the bile drainage was the deciding factor in the alleviation of the jaundice we are not prepared to state. At any rate it must have shortened her period of jaundice and lessened the duration of the liver dysfunction. It is of interest to note the occurrence of the biphasic Van den Bergh reaction with the decrease in bilirubinemia. It seems extremely unlikely that liver-cell damage was greater when the obstruction was relieved than it was when it was absolute. According to the reasoning of Van den Bergh and McNee this is the only tenable explanation for it. In fact, we know that liver dysfunction as gaged by the organs ability to remove dyes from the blood is always greater at the height of the jaundice. Is it possible that the addition of urobilin to the serum in decreasing icterus due to its presence in the bowel is responsible

for the biphasic reaction? Were the giardia in this case responsible for the jaundice? We have nothing to base such a conclusion upon except the marked evidence of duodenitis which was present. Certainly it must be a very rare occurrence, as it was the only case of obstructive jaundice of which we had knowledge in which the flagellate was found. We have observed approximately 30 cases of giardiasis, and duodenitis was practically always present. A re-examination on March 13, 1926 revealed no return of giardiasis four months after the intravenous administration of the arsenical. One large dose of arsphenamin has frequently proved successful in the eradication of this flagellate in our hands.

Case II.—M. R., white, married, female, aged fifty-six, was admitted September 9, 1924. One child dead. Menopause at fifty-two.

Past Medical History.—Negative, except for pneumonia seventeen years ago.

History of Present Illness.—Had slight pain under right costal margin two years ago of several weeks' duration. There is also a history of an occasional spell of slight indigestion for past few years. Both symptoms must have been mild, as they were not elicitated when the history was first taken. About five weeks ago consulted a physician for a "queer" itching sensation in the left thigh and abdomen. One week later she noticed that her skin was yellow. Simultaneously she noted a gray color to stools and very dark urine. She also complained of a heavy feeling in the epigastrium at this time. The icterus has persisted to date and itching has been most annoying, keeping her awake. Thinks she has lost about 30 pounds during past few weeks.

Physical Examination.—Well-nourished woman with moderate icterus. Liver is just palpable on deep inspiration. Slight tenderness in left epigastrium. Chronic arthritis involving fingers. Otherwise examination is negative. Temperature, pulse, and respiration normal.

A case of obstructive jaundice in a middle-aged woman with vague history of slight indigestion and soreness in the upper

right abdomen two years previously. The differential diagnosis has been gone over in Case I. The most likely diagnosis is gall-stone disease or cancer of the pancreas or biliary tract. Her age and the great loss of weight favoring the latter, the previous history of soreness with indigestion and rather sudden onset of the jaundice favoring the former.

The fractional gastric analysis revealed a very marked hyperacidity, the height of the secretion curve being reached seventy-five minutes after the meal, when it was 93 HCl and 110 total acidity. The emptying time was normal. No bile. Gross blood was present in traces in two extractions. Every extraction was positive for occult bleeding. Blood-sugar 125 mg. per 100 c.c. Cholesterol 140 mg. per 100 c.c. Nitrogen normal. Wassermann negative. Erythrocytes 4,250,000. Leukocytes 7800. Hemoblogin 65 per cent. Differential normal. Coagulation time three minutes. The Van den Bergh reaction was indirect, 10 units. The stool was of ash-gray color, loaded with neutral fat, fatty acid, and soaps. Small amount of bile present. Occult blood negative on several occasions. The urine contained a cloud of albumen, bile pigment, and bile salts.

A bile drainage was attempted, but was unsuccessful, the tube not passing through the pylorus. During the attempt, however, considerable bile was regurgitated into the stomach. Microscopically it was found to contain an abundance of tall columnar epithelial cells, which were bile-stained.

x-Ray examination of the abdomen and gastro-intestinal tract was negative for gall-stones. There was evidence of slight cardiospasm. The stomach and cap appeared normal. The second and third portions of the duodenum, however, appeared irregular and did not fill well. The irregularity resembled that frequently found in adhesions.

The outstanding features of the laboratory examinations, which are against the diagnosis of cancer, are: (1) hyperacidity, (2) stools negative for occult bleeding, and (3) the absence of any characteristic defect in the stomach or duodenum which might be due to pressure of a malignant growth. There is a moderate secondary anemia present which might be due to cancer.

The occult blood in the stomach in the absence of blood in the stool bespeaks trauma due to the stomach-tube. There are two features which are worthy of note: (1) Normal blood cholesterol, and (2) indirect Van den Bergh reaction. Both of these findings are unusual in obstructive jaundice. However, there can be no doubt of the obstructive nature of the jaundice with the practically bile-free stools and bile pigment in the urine. The irregularity of the duodenum was very characteristic of that seen in pericholecystic adhesions.

Non-surgical drainage of the gall tract was attempted again on the 17th and 18th. The tube entered the duodenum, but very little bile was obtained. On the following day 100 c.c. of bile was obtained, which contained many flocculations, consisting of pus cells, columnar cells, cholesterin crystals, and bilirubin calcium pigment crystals in abundance. Three days later the procedure was repeated and 400 c.c. of bile was drained having the same microscopic picture. The flocculent débris was more noticeable. At this time the icterus was improving and the stool was almost normal in color.

The medical drainages were given every second, third, or fourth day until October 10th. The icterus was markedly decreased, itching practically disappeared, and patient felt well except for an occasional sharp pain, very short duration, between the scapula. Crystals, pigment, and cells were constantly found. The culture of the bile was reported sterile. Weekly drainages were practised until November 11th, at which time the jaundice had completely disappeared. Then they were given bi-monthly until January 7, 1925. The patient has been drained at infrequent intervals since that time. She has remained in perfect health and was seen one month ago.

The course of the case indicates rather clearly that we were not dealing with carcinoma. We feel rather certain that gall-stones were present. Up to the time of writing we have never encountered a case in which cholesterin crystals and bilirubin calcium pigment were repeatedly found in the bile in which gall-stones or sand were not found at operation. This includes a series of approximately 20 cases to date. We are very strongly

of the opinion that after every diagnostic aid has been exhausted in cases of this sort, and a diagnosis cannot be made, non-surgical gall-bladder drainage, intermittent or continuous, should be instituted before surgery is recommended. If this is unsuccessful after a week or two and the icterus or bilirubinemia is increasing surgery must be recommended. The operative risk is so great in jaundice that medical means of reducing the jaundice deserves a trial when gall-stones are suspected. This patient was seen in January, 1926. There has been no recurrence of symptoms. She feels well, although, of course, an operation will be considered promptly with any return of symptoms. We do not want to give the impression that we consider cholelithiasis a medical disease.

Case III.—C. M., a white, married man, age twenty-five, was admitted March 10, 1924. Chronic gastro-intestinal trouble since he was six years of age. He has been subject to attacks of "biliousness," constipation, coated tongue, nausea, and vomiting every two or three months. Enemas, calomel, and citrate were used frequently, and were helpful. Chronic catarrhal nasopharyngitis existed for years. Frequent attacks of tonsillitis up to age of fourteen, when tonsils were removed. Operation for lymphadenitis followed a short time thereafter. States that he has had a slight icteroid tint to the skin since he was a small boy. The first attack of acute jaundice occurred at fifteen, when he was in bed for three weeks with skin as "yellow as an orange." Jaundice was very intense for two weeks. This attack was accompanied by nausea and vomiting. A second attack similar to this occurred at the age of nineteen. About two weeks previous to admission developed sharp, knife-like pain on the right side of the abdomen extending from the ribs to the umbilicus, of short duration, practically always occurring when on his feet and having no relationship to eating. Pains occurred about twice a week. The appendix was blamed and removed, without relief. These pains still occur. Starting two or three months ago he has been complaining of "wave-like" pains starting under the right costal margin and passing horizontally across

the abdomen to the left costal margin. They occur immediately after meals and last about one hour. The patient lost 39 pounds since 1919. Bowels have been constipated as long as he can remember. They vary in color from normal brown to very "light yellow." At present he also complains of nausea, peristaltic unrest, belching, anorexia, thick taste in the mouth, and offensive breath. There is no itching.

Physical Examination.—Temperature normal. Pulse 82. Blood-pressure 120/75. Weight 130¼ pounds. Height 5 feet, 11 inches. Moderate icteroid tint to conjunctiva, skin, and mucosa of mouth. Tongue coated. Heart and lungs negative. Habitus sthenic. The liver is enlarged, extending down 1 inch below costal margin. Spleen not enlarged or tender.

We are dealing with a case of jaundice of long duration, but probably not continuous. It is unlikely that he was jaundiced at the time of his appendectomy. The patient's father, mother, one sister, and brother are living and well. There is no history of familial jaundice. A history extending back to age of six is very suggestive of hemolytic jaundice, with the acute attacks representing hemoglobinuric crisis. The absence of itching is substantiating, but the lack of enlargement of spleen is definitely against such a diagnosis. Nevertheless chronic hemolytic jaundice of the acquired variety must be considered.

Fractional gastric analysis: Marked hyperacidity in spite of the presence of considerable bile in the stomach. No blood, occult or gross. Emptying time slightly delayed, as evidenced by the overnight retention of microscopic food and undue retention of food two hours after the Ewald meal.

Feces: Alkaline reaction, Light green color. Bile present. Occult blood minus.

Urine: Bilirubin and bile salts negative. Urobilin positive. Indican plus.

Blood: Wassermann negative.

Blood-sugar 98 mg. per 100 c.c.; blood creatinin 1.5 mg.; blood uric acid 3.8 mg.; blood urea nitrogen 15 mg., and blood cholesterol 220 mg. per 100 c.c.

Blood fragility: Beginning hemolysis 0.38.
Complete hemolysis 0.32.

Coagulation time three minutes.

Red blood-cells, 4,790,000. White blood-cells, 9300. Hemoglobin, 80 per cent. Polymorphonuclears, 56. Small lymph., 40. Transitionals, 3. Eosinophils, 3. Large lymph., 1.

Van den Bergh, indirect reaction. Quantitative not done. Widal hemoclasis crisis, postprandial leukopenia. Rosenthal liver function test: fifteen minutes, 5 per cent.
one hour, 5 per cent.
two hours, 0 per cent.

Bile drainage: Fasting acid 50/70. Tube entered promptly (twenty minutes). Fifteen cubic centimeters (15 c.c.) of greenish-yellow bile obtained from duodenum before stimulation. Moderate amount of flocculent material of gastric origin. After two stimulations with magnesium sulphate 245 c.c. of bile was obtained. It contained considerable flocculent precipitate. There was no dark "B" bile. Microscopically there were numerous bile-stained pus cells and moderate-sized columnar cells, all deeply bile stained. Bacillus Friedländer was grown from culture of bile.

x-Ray: High steer-horn stomach. Motility sluggish at first. A spastic incisura was present near the pylorus. No defects in stomach or duodenum. Cap emptied slowly. A number of coils of small intestine were high up in the abdomen on the left side. Some twenty-four-hour delay in the ileum. Forty-eight-hour stasis in cecum. Liver large. Otherwise negative.

Discussion.—The laboratory data supporting a diagnosis of hemolytic jaundice are the presence of urobilinuria, absence of bilirubin and bile salts in the urine, and the indirect Van den Bergh. However, the absence of increased blood fragility and blood-count, the hypercholesteremia and absence of splenic involvement makes a diagnosis of hemolytic jaundice untenable. There is definite evidence of liver dysfunction both by the Rosenthal and Widal methods. The urobilinuria might be likewise interpreted. Since the jaundice is not of the absolute obstruction variety, bile being present in the intestinal tract,

the urobilin can easily be explained on a basis of liver dysfunction. The Van den Bergh reaction is the only laboratory finding which is inconsistent with jaundice due to blood destruction. Our laboratories had only a limited experience at this time, and we must not allow one laboratory examination to outweigh overwhelming evidence in the other direction. More evidence must be produced experimentally before we can rely explicitly upon this test to differentiate the different varieties of jaundice. Several investigators claim that urobilin in the blood will give an indirect reaction. If the urobilin is not the result of blood destruction and these observers are correct, an indirect reaction may not mean hemolytic jaundice. Accepting the contentions of Van den Bergh and McNee concerning the part played by the polygonal cell in jaundice, we should expect a biphasic reaction in this case, since there is probably some obstruction with liver-cell damage.

A long history of nasopharyngeal inflammation and tonsillitis, the evidence of a catarrhal inflammation of the gall tract, and the finding of B. Friedländer in the bile suggest a diagnosis of cholangitis with partial obstruction of the smaller bile-ducts. The absence of bilirubin and bile salts is a little surprising on first thought. The jaundice was not intense, however, and the kidney threshold was probably high. The type of pain is very suggestive of adhesions, another point in favor of an inflammatory condition of the gall tract.

Although we look upon cultures of bile obtained through a duodenal tube with some suspicion, considerable care was taken to avoid contamination in this case. The organism was present in pure culture. The long-standing upper respiratory tract disease may have been the original focus. This organism is only rarely encountered in bile, and might possibly account for the long-standing biliary tract infection which seems obvious.

That we are dealing with a type of chronic jaundice not due to blood destruction, but which must be treated medically, seemed obvious to us. An Einhorn duodenal tube was passed and continuous bile drainage, as suggested by Lyon, was carried out from March 25th to April 2d. We have learned that this plan can

best be carried out when nothing but water is given by mouth. Consequently, five liquid feedings of 8 ounces each were administered into the duodenum daily, using the Einhorn duodenal alimentation apparatus. Thiosinamin, gr. iij was injected daily into the vein for seven days. A vaccine was prepared from the B. Friedländer recovered from the bile. It was administered twice a week. After the continuous bile drainage was stopped on April 2d he was placed on a follow-up cholecystitis régime, *i. e.*, low protein diet, six meals daily, force water, aperients and bile salts, deep breathing exercises, and biweekly bile drainage. One week after leaving the hospital the icterus was not discernible and he was feeling well. Aside from an occasional slight sensation of discomfort in the upper right abdomen he has remained well and has been free from jaundice.

A Rosenthal tetrachlor test three months after leaving the hospital revealed normal liver function. There was no dye fifteen minutes or one hour after injection.

We have found this method of treatment of great value in the treatment of chronic jaundice due to cholangitis and stenosis of the bile-ducts after gall-tract surgery. In cases in which the gall-bladder has been removed, the abdomen full of adhesions, and the ductal system caught up in a mass of adhesions there is little else to offer. Many of these patients will not be cured of their jaundice by any plan of treatment, but continuous drainage will prove to be a life-saving régime in some instances.

Case IV.—T. B., a white married female, was referred from the surgical service of Dr. J. B. Carnett on January 26, 1926. She had a suspension of the uterus and appendectomy eleven years ago. Operation for fistula in ano six years ago. No other illness or operation. Two children living and well. No miscarriages.

History of Present Illness.—Constipation has existed since birth of last child, seventeen years ago. Onset of nausea and pain near the umbilicus eight years ago before eating, relieved by taking food. One year ago she began to have attacks of nausea and vomiting after meals. These "spells" would last for about

six weeks. Some gaseous distention of the abdomen and pyrosis has followed meals occasionally. Soreness between scapula has also occurred at intervals for the past year. Two weeks ago condition became worse. She developed a sensation of marked discomfort in the region of the liver. Gaseous distention, nausea, and weakness caused her to go to bed. At this time she first noticed her skin getting yellow. The stools became very light in color, the urine dark, and itching became severe.

Physical Examination.—Well-nourished woman with very deep icterus. The head, neck, and chest are essentially negative. The liver is palpable about 1 inch below the costal margin. There is some tenderness in the upper right abdomen. Temperature and respirations normal. Pulse 60.

Wassermann negative. Blood-sugar 60 mg. per 100 c.c., urea nitrogen 9 mg., and cholesterol 190 mg. Red blood-cells, 4,350,000. White blood-cells, 7750. Hemoglobin, 85 per cent. Differential shows slight lymphocytosis and 3 per cent. eosinophils. Coagulation time seven minutes. Van den Bergh immediate direct reaction, 70 units. Urine negative except for bilirubin, bile salts, and urobilin. The fasting gastric acidity was high, HCl 40, acidity 50. Two hundred c.c. of lemon-yellow thin bile was obtained by non-surgical drainage of the gall tract after three stimulants were applied to the mucosa. The bile contained many flakes; microscopically, bile-stained pus-cells and columnar cells of the tall variety were present. Golden yellow bile pigment was present in small amounts. No "B" bile was obtained. By cholecystogram the gall-bladder was not visualized using the oral method. The sex, age, symptoms, physical examination, and laboratory tests suggested the diagnosis of cholecystitis with cystic duct obstruction and partial obstruction of the common duct, in all probability due to gallstones. The patient was very intensely jaundiced and her blood contained 70 units of bilirubin, an exceptionally high reading. We advised the surgeon that she was undoubtedly a surgical case, but strongly urged preoperative medical management in order to rid her of icterus if possible and thus cut down the risk of operative mortality. She was drained seven times from Janu-

ary 27th to February 10th. After the first drainage bile flow was copious. Much flocculent débris was present. The fifth drainage revealed a small "B" fraction of bile, as did the two drainages following. We believe we were justified in assuming that the cystic duct obstruction was at least partially relieved because of the appearance of this dark fraction of bile. Bilirubin calcium pigment was not seen after the first drainage.

The Van den Bergh on February 1st was immediate direct 30 units, and on the 8th immediate direct 8 units. Coincidental with the drop in bilirubin there was a marked disappearance of skin icterus. It was almost gone on the 8th. That the common duct obstruction was also disappearing was obvious because of the decreasing icterus and large amount of bile being obtained from the duodenum.

The patient was given three intravenous injections of calcium chlorid after the method of Walters, and operation was performed on February 12, 1926 by Dr. J. B. Carnett. No gall-stones were found. One enlarged lymph-node was situated at the junction of the common and cystic duct. A chronically inflamed gall-bladder was removed. Exploration revealed no other pathology. The patient made a satisfactory convalescence and was discharged feeling well.

Case V.—G. K., aged fifty-five, male, miner. Admitted to hospital January 12, 1926 complaining of "pain in the stomach." History dates back to 1922, since which time he has been having infrequent attacks of pain, pointing strongly toward gall-bladder disease. These attacks came on irrespective of meals and were occasionally accompanied by vomiting. Pain sometimes necessitated calling a physician. Last severe attack came in August, 1925, when he became jaundiced, and this jaundice has persisted to a slight degree since. Since August has been showing attacks of pain about once a month. Lost 26 pounds in past year. The history was obtained with difficulty due to patient's inability to understand English. We did not feel that we could absolutely rely upon his statements.

Physical examination revealed nothing striking except the

presence of a slight icterus. Mouth showed pyorrhea and decayed teeth. Chest was negative. There was a suggestion of an irregular mass under the liver between the gall-bladder and midline. Slight tenderness to palpation in this region. Liver somewhat enlarged. Spleen not palpable.

The qualitative Van den Bergh was immediate direct, the quantitative 7.7 units. Blood fragility hemolysis started at 0.36 and was complete at 0.30, moderate decrease in fragility of the erythrocytes. Blood-count: Red blood-cells, 4,750,000; white blood-cells, 7600; hemoglobin, 94 per cent. Polymorphonuclears 83 per cent. Lymph 14 per cent. Transitionals 2 per cent. Eosinophils 1 per cent. The Wassermann and Kahn reactions were negative.

Blood chemistry: Urea, 25 mg. per 100 c.c.; cholesterol, 164 mg.; sugar, 104 mg.; creatinin, 1.5 mg.

Coagulation time, five minutes.

The liver function was markedly impaired as tested by the Rosenthal tetrachlor method, 7 per cent. retention in fifteen minutes, 10 per cent. in one hour, and 6 per cent. in two hours. The routine examination of the urine was essentially negative repeatedly except for a trace of albumen. Bilirubin and bile salts were absent from the urine. This in spite of 7.7 units of bilirubin in the serum. We have previously mentioned that the kidney threshold for bilirubin is considered to be 4 units in obstructive jaundice. It is probable that the threshold is definitely above that figure in jaundice of long duration. The urine contained definite amounts of urobilin on two occasions. The stools contained bile.

The fractional gastric analysis showed a moderate reduction in acidity and rapid motility. The stomach was empty one hour after the Ewald meal. Bile was present in five extractions.

Four diagnostic biliary drainages yielded the following information: Large gall-bladder fractions were obtained. The flocculent material present consisted of pus and phagocytic cells, undoubtedly of duodenal origin, lamblia intestinalis in the vegetative form, and golden-yellow bile pigment. Gall-bladder visualization by the oral route was attempted. The patient

vomited one hour after the administration of the iodo capsules. The gall-bladder was seen as a very faint shadow fifteen hours after the dye was taken, but was not visualized at twelve hours or after the fat meal. The gastro-intestinal *x*-ray was negative.

The completion of the examinations listed above, which have come to be routine in jaundice cases, left little doubt of the existence of partial obstructive jaundice. Malignancy seemed unlikely in spite of the loss of weight and suggestion of an indefinite mass because of the normal blood-count, lack of evidence of pathology by opaque stomach meal, and the duration of the illness. The biliary drainage indicated the existence of a gall-bladder which functioned, as normal "B" fractions were obtained. The cholecystographic study was unsatisfactory because of vomiting, but a faint shadow was present, negativing a likelihood of cystic duct obstruction. There is no direct evidence of gall-stones in the bladder. In the bile we found two very interesting things—bile pigment and giardia. The latter is our second experience with this flagellate in obstructive jaundice (see Case I). It was associated with the usual evidence of duodenitis, and consequently again brings up the question of the ability to cause sufficient duodenitis to obstruct the ampulla of Vater. In this case, as in Case IV, bilirubin calcium pigment was found. The persistent finding of this pigment in abundance always leans us toward a diagnosis of cholelithiasis. Consequently our feeling at the time was in favor of common duct stone.

A second Van den Bergh on January 22d was immediate direct, 9 units. On January 25th the icterus was increasing. The liver at this time extended three fingers below the costal margin; it was increasing in size. This increasing icterus and progressive enlargement of the liver was occurring in spite of a patent sphincter of Oddi, and ample bile flow by the tube drainage. It is difficult to explain this phenomena on the grounds of increasing obstruction. Our clinical assumption would be that the liver dysfunction was increasing. If this were accounting for the increasing icterus, then it would be natural to expect a biphasic reaction, which was not the case. However, in spite

of this apparent paradoxic situation and in the light of subsequent events, we felt sure that liver dysfunction was actually increasing. The situation here was the opposite of that occurring in Case I, the other case of giardiasis, whose jaundice started to decrease after bile drainage. We felt that the longer duration of jaundice, which was increasing in spite of bile drainage, was a definite indication for surgical intervention. It was recommended, but the patient refused and was discharged. He reconsidered his decision and was readmitted for operation February 8th.

After the usual preoperative care, including calcium chlorid intravenously, the operation was performed February 12th. A large single common duct stone was removed. The gall-bladder was found distended with bile, but seemed sufficiently diseased to the surgeon to warrant its removal. There was a moderate hepatitis and pancreatitis present. The culture from the gall-bladder bile removed at operation showed B. coli and Staphylococcus albus. The operation was performed under gas anesthesia and immediate convalescence was excellent. The pathologic report by Dr. Eugene Case was chronic catarrhal cholecystitis.

The course after operation was stormy. There was ample drainage of bile from the tube up to February 20th, when it was removed, and an abundant flow of bile from the wound afterward. On February 23d the bile became very foul and at times thick, viscid, mucoid bile was present. Culture revealed B. coli infection. The patient developed fever. Starting March 4th thiosinamin, gr. iij, was administered daily for ten days, without apparent benefit. He could retain little food, became gradually weaker. At no time was bile present in the stool after operation. The Van den Bergh remained direct immediate, with 15.6 units on February 18th. Twenty-six units were present March 22d, the reaction again being immediate direct. There was no urobilin in his urine at that time. Bile pigment and salts were present. A jejunostomy was performed March 23d for introduction of food and liquid, which could not be retained, and he improved considerably immediately thereafter, feeling stronger,

with a good pulse. Suddenly at 9 A. M., March 26th, he died. An autopsy could not be obtained.

Comment on Cases IV and V.—The latter case brings up several interesting points. The giardiasis probably had nothing to do with the jaundice. There was undoubtedly an active infection of the gall-bladder and biliary tract at time of operation. The failure of bile to appear in the bowel after operation in spite of its presence there before we cannot explain. Before operation there was urobilin in the urine and bile in the bowel. After operation when there was no bile in the bowel urobilin was never found in the urine. Thus, in spite of the marked cholangitis after operation, urobilin was probably not formed in the biliary tract. Before operation the amount of bilirubin in the blood was relatively small as far as jaundice cases are concerned. The Van den Bergh was immediate direct and the obstruction was incomplete, but urobilin was present in the urine. After operation, in the absence of urobilin from the blood-stream, but with marked evidence of liver dysfunction of long duration, the Van den Bergh remained immediate direct.

This case is against the possibility of urobilin influencing the Van den Bergh reaction. If the contention of Van den Bergh and McNee is correct we should have expected a biphasic reaction, owing to the marked disturbance of liver function which was present. The liver inspected after death showed evidence of advanced hepatitis, having a deep purple mottled appearance. After operation no bile reached the intestine, from 10 to 30 ounces of bile drained outside the body daily. The food intake was insignificant. In spite of this, intense icterus was present. This emphasizes the insignificant part played by the kidney in excreting bile from the body.

The 2 cases described above were operated upon the same day. Both had obstructive jaundice with symptoms of several years' duration. Case V had mild jaundice of long duration and Case IV intense jaundice of short duration. Both had bilirubin calcium crystals in the bile. Although the jaundice had practically disappeared in Case IV, we anticipated a finding of gall-

stones in both instances. Case IV had no stones and only mild cholecystitis. She received a preliminary medical treatment, which might have been adequate for her ultimate relief in the light of her operative findings.

Operation at least could have been indefinitely postponed, as it was in Case II. How are we to ascertain which of these cases should be sent to a surgeon and which is to be treated medically? The disappearance of bilirubin calcium pigment crystals from the bile may be a point of note. In our experience a persistence of this pigment with cholesterin after repeated drainages practically always means gall-stones. Case V had the pigment constantly in the bile after each drainage. Of course, it is true that the majority of cases, like Case IV, will prove to have gall-stones and will require surgery. In cases in which the blood bilirubin is decreasing under medical management, surgery had better be postponed at least until the icterus has disappeared. Whether it should be resorted to at all will depend upon the individual case. All jaundice cases are primarily medical, and the keenest judgment is often necessary to decide when to resort to surgery. The quantitative blood bilirubin estimation and the duodenal tube are the most important instruments at the disposal of the internist who is experienced in their use and the interpretation of data obtained from them. If the blood bilirubin remains stationary or increases in spite of medical treatment, too much time must not be lost in calling the surgeon.

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CHRONIC ARTHRITIS

DURING the past ten years the subject of chronic arthritis has interested a great many of the medical profession. Probably in no disease has greater advance been made. It is a fact thoroughly established that chronic arthritis is of infectious origin and everyone realizes the importance of focal infection. Marked strides have been made to alleviate the symptoms of the chronic arthritic patients. The mode of onset, the progression of the disease, the occurrence of fever, leukocytosis well establish the fact that this disease is of infectious origin. The vast majority of these cases start with swelling of the smaller joints, mostly the metacarpophalangeal and the metatarsophalangeal. The process may be unilateral at the start, but usually becomes bilateral as the disease progresses. In the early stages the joints gradually swell, with little or no pain. This gives them the characteristic fusiform appearance. At this time only the soft tissues around the joint are involved. Upon examination, they have a distinct doughy feeling. At times there is a questionable effusion in the joints. Pathologically, this enlargement is due to swelling and hypertrophy of the synovial membrane and capsular ligaments. Pain is only present upon pressure and active or passive motion. The disease progresses with definite periods of acute exacerbation, characterized by fever and its accompanying symptoms, increased pain, stiffness of the joints and the surrounding structure. Frequently there is increased swelling and redness in the joint structures themselves. These periods are always associated with a slight increase in the leukocyte count as compared to the stage during the quiescence. During the acute ex-

acerbations fever is practically always present, even though it be of small magnitude. During this time the disease progresses upward, involving the larger joints, namely, the wrist, the elbow, shoulder, ankle, knee, hip, and joints of the spine.

Soon after the beginning of the process, which in itself is essentially a hypertrophy of the periarticular structures, we have an atrophic process set up. This involves the muscles, subcutaneous fat, and skin. These changes are undoubtedly due, in many instances, to a reflex atrophy. Volpain's idea, namely, an impulse carried from irritated articular nerves alters the trophic activity of the cells in the anterior horns without causing a lesion, but sufficient to cause atrophy and weakness, is an extremely good one, and is the best explanation offered for this process. It is because of the atrophic condition of the skin, atrophy of the subcutaneous fat and muscles, plus their subsequent contraction, which gives the characteristic deformity of this disease. The extensor group of muscles always suffers greater damage than the flexor group and flexor contracture always predominates. This is explained by the fact that nerves which supply the extensors also supply the joints themselves. Consequently, they bear the brunt of the irritation to a greater degree. Associated with this degenerative process is a fibrositis involving both the aponeurosis and the muscles themselves. In fleshy individuals the subcutaneous fat is also caught in the process in the form of a panniculitis. These two conditions account for a good deal of the patient's suffering and will form a very important part in the treatment.

The term "chronic arthritis," as here used, designates a large group of cases which have been formerly classified as chronic non-suppurative arthritis, rheumatoid arthritis, chronic infectious arthritis, chronic osteo-arthritis, or arthritis deformans. This wide classification is made for the purpose of simplicity. If one studies the pathology of these joints, he will find that atrophy and hypertrophy takes place simultaneously. Consequently, it is ofttimes impossible to make a decision which predominates and, therefore, a suitable classification. Gout or gouty arthropathy, being a purely metabolic disease, is not here considered.

The same holds true of arthropathies of nervous origin or those occurring in tabes dorsalis (Charcot joint) and syringomyelia. The chronic hypertrophic osteo-arthropathies occurring in the course of pulmonary tuberculosis, bronchiectasis, chronic bronchitis, malignant tumors of the lung, and various chronic cardiac conditions are again distinct and are not included in the above term—chronic arthritis. Syphilitic arthritis is again a more or less distinct entity and is not here considered. This, however, does not include that group of cases who have a definite chronic arthritis with an associated underlying syphilitic infection. Villous arthritis is probably a stage of chronic osteo-arthritis and will be considered as such. Chronic spondylitis or spondylitis rhizomelica is a definite form of chronic infectious arthritis and will be included in this series of cases.

The analysis of the material submitted comprises the study of 186 cases. Realizing the complexity of a chronic arthritis, we have endeavored to look at these cases from all angles and wherever possible to find sources of infection. This, however, in many was an absolute impossibility.

CHART 1—AGE INCIDENCE

	Cases.	Per cent.
Under 20 years of age	2	1
20 to 30 years of age	22	12
30 to 40 years of age	36	20
40 to 60 years of age	97	51
60 years and over	30	16

As you will note from the above chart, practically no age is exempt from this type of disease. It is, however, a disease comparatively rare under the age of twenty. When it does occur, it is of an extremely virulent form. The majority of cases occur past middle life. This includes a great group of cases which have been termed "metabolic arthritis." They occur after or at about the time of the menopause. This fact, however, does not have an etiologic factor. Many of these women have had symptoms for several years prior to the occurrence of the menopause. During the menopausal stage the patient's resistance is lowered and the disease has an opportunity to progress more rapidly.

CHART 2—PROBABLE SOURCE OF INFECTION

	Cases.	Per cent.
Intestinal tract	70	37
Tonsils	66	35
Teeth	39	20
Gall-bladder	25	13
Sinuses	6	3
Prostate	2	1
Unexplained	Approximately	5

In the studying of this classification of probable sources of infection we wish to call to your attention the fact that the vast majority of these patients have been going the round of various types of specialists before consulting us. Consequently, the sources of infection have been removed. Owing to this fact infections of the mouth and upper respiratory tract occupy a less important part in this analysis. In searching for focal infection let us bear in mind that the vast majority of these cases are of multiple foci rather than one single focus. It is for this reason that we ofttimes fail in getting the desired result after the removal of diseased teeth, tonsils, etc. Another point of extreme importance to remember is that after the primary focus has been removed, the lymphatics which drained this area of infection still harbor the organism and may still be an infecting factor. Teeth and tonsils correctly occupy the foreground as the most frequent site of focal infection in the vast majority of cases. Following these are the sinuses, gall-bladder, prostate, infected ingrown toe-nail, ulceration along the intestinal tract, mediastinal lymph-nodes, etc. The female pelvis in our series of cases has not been found an important factor. In all cases, especially those involving the lower portions of the spine and sacro-iliac joints, the prostate and the seminal vesicles are to be examined with great care. Ofttimes the first massage of the prostate will fail to show any evidence of infection, but upon a subsequent examination a definite prostatitis will be found to be associated. When found, as a source of infection, we are too prone to look upon it as a gonorrheal type of disease. The streptococcus may long persist without any gonococci being found. Non-surgical biliary drainage done in an aseptic way may afford many oppor-

tunities for the study of the gall tract for infection. With the wide use of the Graham test one will have a very valuable asset in the study of gall-bladder disease. In this group of cases the intestinal tract has acted as a probable source of infection in 70 per cent. A great many of these were in the form of visceroptosis and intestinal stasis. Forty-five per cent. of our cases were of normal weight according to age, height, and sex. Of these cases, 4 show evidence of visceroptosis and stasis. Only 15 per cent. of our cases were overweight. Two of these show an acquired visceroptosis. Forty-three per cent. of our cases were underweight; of these, 60 per cent. showed definite evidence of ptosis and stasis. It is for this reason that the gastro-intestinal tract forms a tremendous factor in the care of the arthritic patient. In our experience the diet is of importance only inasmuch as it has to do with the gastro-intestinal tract. The gall-bladder is again extremely important. In this series 25, or 15 per cent., showed definite evidence of disease.

As before mentioned, a great many of these cases having been studied elsewhere before coming under our observation, tonsils and teeth occupy a less important phase than the gastro-intestinal tract. The studies occupy an extremely small part. We might state that in the sinus work all cases, irrespective of whether having symptoms or not, were transilluminated, and if any cloudiness was found whatsoever, the sinuses were *x*-rayed. This was done to obviate any possibility of overlooking any hidden infection. The prostate was found to be a source of infection in only 2 cases. This is probably due to the fact that a great portion of these patients were females. In the tonsil work we wish to call attention to the fact that lymphoid tissue, which ofttimes regrows in the tonsillar fossæ or bits of tonsillar tissue which remain, may harbor rich growths of streptococci and act as a focus of infection. When examining these cases you find injected tonsillar pillars and possibly small cervical adenitis, one should never be satisfied until after making tonsil cultures from these apparent benign lymphoid growths. Tonsillar cultures may not be of any great clinical use because of mouth infection, especially during the winter months when the

so-called "colds" and sore throats are so prevalent. However, when rich growths of streptococci are obtained, it is an additional link in the chain of evidence in condemning that portion of the patient's anatomy. The prevalence of Streptococcus viridans and Streptococcus hemolyticus is about equally proportioned in these cultures.

CHART 3—BLOOD-PRESSURE

	Cases.	Per cent.
Normal	93	54
Hypertension	16	9+
Hypotension	64	37

Ninety-three cases, or 54 per cent., showed a normal blood-pressure. The hypertension cases occupied a very small portion, or 9 per cent. In this group occurred cases of benign hypertension, generalized arteriosclerosis, and chronic nephritis. The hypotension cases occupied a rather large percentage—37 per cent. It is interesting to note that 75 per cent. of these hypotension cases were of the visceroptotic variety, the hypotension, in all probability, being only a part of their general condition.

(Note: These blood-pressure readings were based upon a normal pressure—120 systolic in an individual twenty-one years of age. One-half point was added for each additional year of the patient's age.)

CHART 4—BLOOD-COUNT

	Cases.	Per cent.
Normal	128	70
Secondary anemia	48	30
Leukocytosis	18	10
Leukopenia	43	24

Normal count:	Red blood-cells	4,000,000
	White blood-cells	6500 to 9000
	Hemoglobin	80 per cent.

It is surprising the large number of patients who have an absolutely normal blood-count in this type of disease. In this group 128 cases, or 70 per cent., showed a normal count. In 40 cases we had a secondary anemia of moderate degree. In 18 of our cases we had a definite leukocytosis. The vast majority

of these cases were examined during a period of acute exacerbation. Forty-three cases, or 42 per cent., showed a definite leukopenia. The differential count in these leukopenics showed a relative increase in the number of lymphocytes. It has been our experience that during the period of quiescence a lymphocytosis exists, while during the period of acute exacerbation the leukocytosis gives way to polymorphonuclear variety.

CHART 5—BLOOD CHEMISTRY

	Cases.	Per cent.
Normal:		
Blood-sugar	142	86
Blood-urea nitrogen	138	78
Blood-uric acid	138	84
Blood-creatinin	124	98
Blood-calcium	20	100
Above:		
Blood-sugar	12	7.5
Blood-urea nitrogen	32	18
Blood-uric acid	24	14
Blood-creatinin	3	2
Below:		
Blood-sugar	10	6
Blood-urea nitrogen	5	4
Blood-uric acid	3	2

		Mg. per 100 c.c. of blood.
Calculated normals	Blood-sugar	80–120
	Blood-urea	14– 17
	Blood-uric acid	2– 3.5
	Blood-creatinin	1
	Blood-calcium	9– 11.5

Blood chemistry in this type of case is of extremely little value. You will note from the above chart that the vast majority of the cases have an absolutely normal chemistry. With the hypoglycemia, which others have reported to find in this type of case, we did not concur. This may be explained by the fact that we allowed a wide variation—between 80 and 120 milligrams per 100 c.c. of blood—as a normal. In 12, or 7.5 per cent., we found a definite hyperglycemia. Several of these were

potential diabetics. Like the blood-sugars, the urea nitrogen was of very little importance. Thirty-two, or 18 per cent., of our cases had a slight retention. This, of course, occurred in patients showing other evidence of chronic nephritis. Uric acid estimations were useful in helping us to differentiate between cases of chronic arthritis of infectious origin and those of metabolic origin. In 24, or 14 per cent., we found the uric acid above normal. In several of these we had a combination of the two conditions existing. This condition may be overlooked if it were not for the persistent high uric acid in the blood. Because of the very few cases of chronic nephritis being associated creatinins were normal in all except 3, or 2 per cent. Thinking that there might be an increase in the amount of blood calcium in these patients because of the marked exostoses occurring, we have endeavored of late to determine the blood calcium. Here, as in all of the blood chemistry, we found a normal calcium in 20 of our patients. This comprises all the calciums that have been done in this group. As far as we can tell from such a small series, there is no alteration in the calcium content of the blood in chronic arthritis.

CHART 6—GASTRIC CONTENT

	Cases.	Per cent.
Normal	32	40
(Free HCl 20–40)		
Total HCl 40–60		
Hyperacidity	26	30
Hypo-acidity	12	14
Achlorhydria	14	16

Fractional gastric work was not done in cases which did not present symptoms. The Ewald test-meal was used in all cases and extraction was made by the fractional method. The titration was done immediately after the extraction. Six to eight specimens were collected over a two-hour period in every case. As you will note from the above chart, 32 cases, or 40 per cent., showed a normal curve. Twenty-five cases, or 30 per cent., showed a marked hyperacidity. Twelve cases, or 14 per cent., showed a diminution in the acid content. In 14 cases we had an

absence of hydrochloric acid throughout the entire two-hour period. These may not be true cases of achylia gastrica because ferments were not tested, and for that reason the term "achylia gastrica" has not been used.

Additional metabolic studies as well as sugar tolerance tests have been done routinely upon many of this group of cases. The results obtained were very varied and did not lend any additional information as to treatment. Several of the overweight cases showed increased metabolic rate. Many of the undernourished, underweight cases showed a decreased metabolic rate. In some of the overweight cases a positive sugar tolerance test was obtained. This, then, was of value in the correction of the patient's diet. Routine Wassermanns should be done because an underlying syphilitic infection will ofttimes prevent getting the desired result in other forms of treatment. It has been our experience that a patient who has a chronic arthritis with an underlying syphilis will not improve from an arthritic standpoint until the syphilis has been entirely eradicated. Stool examinations are again of only moderate value. Their primary importance is in relationship to the gastro-intestinal tract and not to the arthritis.

MODE OF TREATMENT

Treatment is not started upon any of these cases until after a very thorough and exhaustive study has been made and all foci of infection have been removed. These patients are usually placed in hospitals for a short time during the starting of the vaccine. Rest in bed is a very essential element in these cases, and a few weeks in bed usually affords benefit. This is of primary importance in the undernourished case, especially the visceroptosis. The foot of the bed is elevated 9 inches and the patients are encouraged to lie upon their right side to hasten gastric emptying after each meal. The diet in all these cases is one suitable for the gastro-intestinal findings. In the undernourished variety six meals a day are usually given if the patient can at all tolerate them. These diets are usually high in fat and we are fond of giving the patients cream and Celestine Vichy in equal parts between meals. In so doing we can usually get

the patient to take 8 to 12 ounces of cream per day without any gastric discomfort. If there is any evidence of intestinal stasis, colonic irrigations are given, washing out the colon with 8 to 12 quarts of water. This is usually repeated twice a week. If the patient is at all ambulatory, a Rose belt is applied to hold up the colon during the time they are out of bed. Patients do not complain of the adhesive plaster, but are usually gratified with the sense of support that they receive. Patients usually gain weight more rapidly when such support is worn. When the skin becomes sensitive various types of abdominal belts and corsets are then used. The choice of belts and corsets depends a great deal upon the type of abdomen with which you are dealing.

Along with the general care of the gastro-intestinal tract in such a manner, we routinely give iron and arsenic or sodium cacodylate hypodermically. Even though the patient has a normal blood-count, the iron and arsenic seems to give them additional tone. Electrotherapy in the form of electric bakes and hydrotherapy in the form of hot and cold compresses, etc., are used routinely in all cases. It must be remembered, however, that in a few this type of treatment will aggravate the condition, and if found to do so, should be discontinued immediately. It has been our experience that massage should be started rather late in the disease. The muscles are too inflamed to be massaged at the start. We encourage our patients to get as much motion in the affected extremity as possible, thinking that the active motion obtained is by far more beneficial than the passive. At the same time the patient will not, because of the pain, damage the joints. The overenthusiastic masseur is very apt to cause damage to the inflamed joint. The contractures are to a great extent overcome by the patients themselves. This is done by hyperextension without weights. Mechanical applicances are not used until after the patient has endeavored by exercise and hyperextension to strengthen his own joints. Buck's extension and braces with thumb-screws are placed upon patients who otherwise are unable to break up the associated fibrositis.

In addition to the above general care of these patients, we have for the past ten years used foreign proteins in the form of

Coley's fluid. Coley's fluid was selected because of its high-powered potency plus the fact that it is always easily obtained upon the market. We feel that in the use of foreign proteins in these cases the most benefit is derived by repeated small protein stimulations and not by generalized reactions. Consequently, in all cases we have been inclined to keep the dose extremely small, in many cases not exceeding 3 or 4 minims at the end of a year's treatment. We have also noted that as the vaccine is continued over a long period of time the people seem to become hypersensitive to it and it is necessary to reduce the dose. In starting the vaccine it is, therefore, very essential to start with a small dose—usually $\frac{1}{4}$ minim in 1 c.c. salt solution or sterile water. This is given subcutaneously. Three types of reaction are experienced—focal, local, and general. It has been our experience to tell these people that after the vaccine injection they will have pain in joints heretofore unknown to be involved. The pain in the joints is invariably increased after the first four or five injections. This, thereafter, will gradually be diminished and the period of freedom from pain will gradually be increased. At the site of injection a marked erythematous area develops. This fluid is quite irritating, and at times you will think of abscess formation. This we have not experienced, but for a week or more the hard indurated nodules persist. These patients are very hypersensitive to the vaccines and the dose must be increased very slowly. This hypersensitivity persists surprisingly throughout the course of treatment and varies with each individual. The largest dose of vaccine given was 10 minims and that after eight months' treatment. In a case of fifteen years' duration in which we obtained a beautiful result, we could never give over 4 minims without causing a general reaction. It is to be remembered that in these long-standing cases the patients are usually anemic and markedly undernourished. The pain has been severe and their nerve is broken. Consequently, it is important to try and avoid a general reaction. While this does not do the patient any harm, it is bad from a psychologic standpoint. In addition, they have been through so many hands and tried so many forms of treatment that they are always dubious

of any new treatment, and especially so if they are to have more pain in the beginning.

The time interval of the injections varies from three to four days at the beginning, gradually being lengthened to five or six days as the symptoms improve. It has been our rule to gage the time of injection and the size of the dose entirely upon the local reaction. If it be severe, the same dose is repeated. At times it is necessary to repeat the same dose as many as four or five times before increasing the vaccine. Especially is this true as the larger doses are used. The vaccine is continued until the patient is clinically well. Unfortunately, the time of stopping the vaccine is entirely empirical, as we know of no way of telling when the infection has been entirely killed out.

The benefits derived are diminution of pain plus a loosening of the joints. The acute exacerbations which are so characteristic of the disease are gradually diminished and are finally obliterated. It is remarkable to see the rapidity of diminution in the size of the joints. The patient through his own efforts will begin to move the joint and loosen it up as soon as the pain subsides. In the febrile cases the temperature gradually returns to the normal course. The patient's general health improves and he soon loses his toxic apparance. The gain in weight is quite remarkable. One patient who has been under treatment for the past seven months has gained 42 pounds.

In conclusion, it must be said that the treatment of these cases is as complex as their source of infection. The more thoroughly they are studied, the more frequently we believe we will find definite evidence of streptococcus infection. Unfortunately, the streptococcus does not lend itself to the formation of the agglutinins or precipitins. Consequently, serologic tests so far have failed to give us any definite information. Coley's mixed toxins, when used cautiously and over a prolonged period of time, have, in our hands, given us satisfactory and pleasing results.

CLINIC OF DRS. F. C. KNOWLES AND JOHN B. LUDY

PENNSYLVANIA AND PHILADELPHIA GENERAL HOSPITALS

PELLAGRA AS OBSERVED AT THE PENNSYLVANIA AND THE PHILADELPHIA GENERAL HOSPITALS

SINCE 1920 we have had occasion to observe 65 cases of pellagra, 15 of which were diagnosed as pseudopellagra.

Our first house cases at the Pennsylvania Hospital were observed in 1922.

In the years prior to 1915 a sporadic case would occasionally appear in our Out-patient Department, but in the years following we have observed them more frequently and in increasing numbers.

Some of our cases which were diagnosed as pseudopellagra later found haven in the wards with classical symptoms of pellagra. We, therefore, opine that pseudopellagra and pellagra are the same, differing only in degree.

Pellagra is either an acute or chronic constitutional disease characterized by dermatitis, diarrhea, and cerebral disturbance, and having a tendency to seasonal recurrence.

The dermatitis is always symmetric and is diagnostic of the disease.

The lesions *ab initio* consist of large macules which coalesce to form mahogany colored patches not unlike sunburn. As the disease progresses the patches assume a dark red hue and in from one to two weeks desquamate, leaving a more or less pigmented surface. The lesions are limited for the most part to exposed surfaces, as the dorsum of the hands, forearm, face, neck, and scalp. The feet and ankles may be similarly affected. In the acute cases vesicles and bullæ may be present and a secondary

infection may complicate the same. Ecchymosis has also been noted.

Sunlight undoubtedly influences the location of the skin lesions. Those patients to whom either coat or shirtsleeves are taboo invariably show involvement of the forearms, while in the fully garbed individual the lesion ends abruptly at the wrist.

After repeated attacks the skin becomes more or less permanently thickened, scaly, and pigmented.

Subjective symptoms are, for the most part, absent.

The gastro-intestinal symptoms are those of gastro-enteritis. Diarrhea is the rule, although constipation and diarrhea may be alternately present.

The stools have a foul odor and frequently contain mucus, blood, and undigested food.

The tongue is usually dry, redder, and smoother than normal. In the more severe cases it is denuded of its epithelial covering and harbors yellowish superficial sloughs.

The nervous system exhibits symptoms commonly seen in toxemia. Liability to delirium is common.

The course of the disease is variable. It is more apt to occur in the spring or fall, continue for a period of six weeks, and then return to normal and recur the next spring.

The average duration is about five years. The ultimate outlook in a classical case of pellagra is grave.

According to Joseph Goldberger, Surgeon, U. S. P. H., the primary etiologic dietetic factor is a faulty protein (amino-acid) mixture, a deficiency in some as yet unrecognized dietary complex (possibly a vitamin) or some combination of these.

The symptoms point to a toxemia, the origin of which is the intestinal tract.

Fresh meat and milk, with a liberal supply of vegetables, constitute the treatment rationale. By way of medication, yeast, arsenic, and citric acid have been favorably regarded. Weekly intravenous injections of tryparsamid (2 gm.) were of decided benefit in several of the cases.

The following cases aptly demonstrate the symptoms and course of the disease:

Case I.—T. D., white male; laborer; age fifty-one; American.
Admitted 9/24/23. Diagnosis: Pseudopellagra.
Discharged 10/17/23.
Re-admitted 4/16/25.
Discharged 6/3/25.
Re-admitted 10/13/25.
Died 10/24/25.

Previous History.—Patient was admitted to hospital 9/24/23 for alcoholic pseudopellagra. Two months prior to present admission he invested largely in bad liquor and proceeded to consume it. Three weeks before admission patient's hands became red and swollen and a few days later developed a crop of blisters on them. His tongue was swollen and sore and he had dysphagia. History stated that his hands were exposed to old musty corn.

Physical Examination.—Patient is greatly emaciated. Dermatitis of the hands, limited to the dorsal surface. Face and neck as well as hands show a brownish coloration. Face shows a powdery exfoliation. Tongue is swollen and beefy red. Mucous membranes are greatly congested and harbor many sloughs. No dementia, no diarrhea. Discharged as improved 10/17/23.

Readmitted 4/16/25. States that dermatitis began two weeks ago associated with loss of appetite and diarrhea.

Physical Examination.—Patient greatly emaciated; skin of the neck shows a dark red pigmentation. Dorsum of the hands shows a marked dermatitis resembling a "sunburn." On 4/19/25 the dermatitis developed on the cheek and nose. Leukocytosis of 23,000. Slight eosinophilia. Patient was discharged improved 6/3/25 with a diagnosis of pellagra.

Re-admitted 10/13/25.

History of Present Illness.—Patient has had diarrhea, intermittent in character, for the past two years. He states that the back of his hands have been inflamed and pigmented on and off for a number of years, but that lately they have been darker than formerly. He came to the hospital because of a sore mouth which has been present for three days and has greatly interfered with deglutition. Later notes show the patient became irrational

and disoriented. Later he became delirious and had hallucinations. He died 10/24/25. Diagnosis: Pellagra.

Autopsy showed an acute enteritis; edema of the brain with marked dilatation of the ventricles.

(N. B.: This patient when first admitted had a so-called "pseudopellagra." He had a pellagra at that time.

Case II.—F. K., white; age forty-seven; born in Ireland; laborer. Admitted 6/9/24.

Previous History.—No history of prior illness obtainable; patient has been a heavy drinker during the last five years and had been on a "spree" for several weeks prior to his first admission, 3/26/24. At the time of his first admission his chief complaint was diarrhea and loss of weight. No note made of any dermatitis; however, patient states that he has been subject to attacks of "sunburn," more so during the last several years, which affected his hands more than his face.

On his second admission, 6/9/24, patient showed evident symptoms of pellagra.

The dorsum of both hands were scaly and pigmented, resembling in color dark mahogany; face showed slight dermatitis, as did also the neck.

Diarrhea was pronounced—fifteen to twenty stools per day. Patient was emaciated and had lost about 40 pounds. Knee-jerks exaggerated. Patient states his limbs were more or less trembling.

Laboratory examinations were negative, except the gastric analysis disclosed absence of free HCl, and but very little total acidity.

Feces showed occult blood.

Patient died July 26, 1924.

Autopsy.—Intestines showed an acute enteritis and a chronic ulcerative colitis.

Case III.—C. H., age forty-eight; white; laborer; American. Admitted to Philadelphia General Hospital May 21, 1926.

Patient first appeared in Out-Patient Skin Clinic of Pennsylvania Hospital early in March, 1926. At the time of this visit

he showed a bilateral dermatitis on dorsum of both hands which was sharply marginated and terminated abruptly at the wrist (gauntlet fashion). The face and neck showed a similar dermatitis. The picture greatly resembled sunburn.

The edge of tongue at this time was red and minus its epithelium.

No diarrhea; no mental symptoms present.

Previous History.—Patient had never been ill. Confesses to the usual diseases of childhood, but does not remember which ones.

He further confesses to being a free user of alcohol and states that for twelve years he had used it daily, and that for the past eight months he outdid himself in this accomplishment, being constantly more or less intoxicated.

He recalls having had similar attacks of "sunburn" about the same time of the year for several years. He says he wouldn't have bothered this year only that his hands felt so numb.

Patient continued as a dispensary patient until May 21, 1926, when his condition became quite alarming. During the few weeks prior to admission he developed a diarrhea which became more and more distressing, and being now convinced of the uselessness of alcoholic therapy he consented to go to the Philadelphia General Hospital.

At the time of admission to hospital patient had lost about 30 pounds in weight and was decidedly asthenic.

Patient had from fifteen to twenty stools per day.

His tongue was dry and swollen.

Pharyngeal and buccal mucosa harbored many superficial yellowish sloughs.

Dorsum of hands showed exfoliation and dark red pigmentation. Face also showed a branny exfoliation, but less pigmentation. He was extremely restless and complained of insomnia and vertigo, especially marked early in the day.

Patient was discharged at his own request June 22, 1926.

At time of discharge diarrhea had stopped and except for pigmentation of hands he appeared normal.

Case IV.—E. B., age forty-eight; white; American; Morocco worker.

Admitted 8/27/23.

Patient has been a moderate drinker since the age of eighteen.

No history of previous illness.

Present History.—Patient was in good health until two weeks ago, when his hands became "chafed and tight, with a burning sensation." Four days later he developed shooting pain in his stomach with diarrhea. Had six watery stools per day and is growing worse.

Physical Examination.—Patient has a very foul breath. Tongue is beefy red, with yellowish superficial sloughs. The dorsa of hands show bilateral glove-like dermatitis and are dark red in color. Elbows show small areas of dermatitis, as does the right shoulder.

September 10, 1923: Hands were fissured and scaly; patient complains severely of the burning sensation in them, and also complains of difficulty in swallowing. Patient is slightly depressed; however, diarrhea has ceased.

September 20, 1923: Patient developed a temperature and has delusions of persecution and talks to himself continuously.

Diarrhea, dermatitis, and glossitis were very pronounced at this time.

Patient died September 27, 1923.

Autopsy.—Intestines show atrophy and petechial hemorrhages. Acute ulcerative and hemorrhagic enteritis. Stomach shows chronic catarrhal gastritis. Brain large, heavy, with generalized convolutional atrophy. Edema present.

Case V.—Henrietta W., age forty-two; negress; housework. Admitted 5/7/23.

Patient's first symptoms began six or seven months ago, with burning and itching of the feet, followed a few days later by the same trouble with her hands. At the same time she had diarrhea. She treated her hands and feet with home remedies. About four months ago she noticed that her hands and feet were darker than the rest of the body.

Physical Examination.—Shows dermatitis of hands and forearms extending to the elbow. Dermatitis is also present on dorsum of both feet and in the inguinal region.

Notes of the first week in July, 1923, state the patient is confused, delirious, and hallucinated. Patient became progressively worse and died July 23, 1923.

Blood-count on May 16, 1923 showed a slight secondary anemia and leukocytosis of 30,000.

Autopsy shows pellagra of the skin, gastro-enteritis, with pigmentation of the colon; brain and cord normal except for slight posterior column degeneration.

Case VI.—H. Mc., age sixty-four; white; American; gardener. Admitted 10/5/25.

Patient has been a free user of alcoholic beverages for fifteen years.

Patient states four months ago he was "sun-poisoned" on his hands and forearms. They became swollen, red, and later scaly. About two weeks previous to admission same thing occurred on his neck. Four weeks ago he developed a watery diarrhea—fifteen to twenty-four stools per day.

Physical Examination.—Dermatitis and pigmentation of face, neck, forearms, and dorsal surface of hands. Ankles and feet show presence of dermatitis, although not so pronounced. The tongue is swollen and beefy red.

Knee-jerks are exaggerated.

Patient was given a liberal diet of fresh vegetables, fresh meat, and milk.

Patient began to improve.

Discharged January 16, 1926.

Diagnosis of alcoholic pseudopellagra had been made at time of admission.

Case VII.—Margaret S., age twenty-six; colored; housework. Admitted 11/29/25.

Diagnosis.—Pseudopellagra.

Patient gave a history of having daily imbibed ½ pint of gin or whisky since early childhood.

Complains of loss of appetite, loss of weight, weakness, and diarrhea.

Patient states that she has had more or less stomach trouble and diarrhea for past two years.

Physical examination shows a swollen red and beefy appearing tongue. Buccal mucosa and pharynx are congested.

Skin on dorsum of hands is thickened, scaly, and darkly pigmented.

Knee-jerks are absent. Patient is disoriented and has hallucinations. She became progressively weaker and died December 26, 1925. No autopsy.

Case VIII.—Grace C., age thirty-seven; colored; married. Admitted 2/5/25.

Patient has had nausea, vomiting, and diarrhea for last nine months. Has been in bed for last six months.

Five months ago developed pain in her hands which was followed by signs of inflammation, and still later by peeling and discoloration. The skin over both breasts and anterior chest wall extending to neck and shoulders is thicker than normal, deeply pigmented, and desquamating. (Condition referred to as "Necklace of Casal.")

Physical Examination.—Patient has from twelve to fourteen watery stools per day. Has lost about 16 pounds in weight. Does not remember very well and her mind seems to wander.

Dorsum of hands and dorsum of feet show thickening, hyperpigmentation, and desquamation.

Reflexes absent. Pain sense diminished below the knees.

Note February 19, 1925 states that patient is hallucinated and has delusions of persecution. Has choreiform movements of hands and arms.

February 20, 1925 had a convulsion, followed by stupor.

Patient died March 2, 1925.

Autopsy shows acute congestion of duodenum, with small patches of congestion throughout the intestines.

Conclusions.—Of the 50 cases of pellagra that found haven in a hospital ward during the last five years, 32 have died and 18 have been discharged. Autopsy was done in 14 cases.

All cases on whom a gastric analysis was done had no free HCl and a low total acidity.

A large majority of cases gave a definite history of alcoholism.

The cutaneous eruption must be differentiated from erythema multiforme, sunburn, and chronic eczema.

From erythema multiforme it is distinguished by the changes in the skin which persist after the acute attacks have subsided, and the concomitant nervous and gastric intestinal symptoms.

From chronic eczema it is distinguished by the absence of itching, the presence of mucous membrane involvement, and the characteristic distribution of the eruption.

Solar dermatitis usually subsides in about forty-eight hours and is followed by desquamation and a transient pigmentation.

There is also an absence of mouth involvement in sunburn as well as other consitutional symptoms.

From our observations we conclude that pellagra is on the increase in Philadelphia.

CLINIC OF DR. MARTIN E. REHFUSS

JEFFERSON MEDICAL COLLEGE

ORGANIC DUODENAL PATHOLOGY

CLINICIANS concentrate on the stomach not infrequently to the exclusion of the duodenum. This is an unfortunate tendency which at times is liable to lead us to an erroneous diagnosis. The explanation of many of the interesting phenomena of unexplained gastric and upper digestive conditions is to be found in the duodenum. While the stomach is undoubtedly a barometer registering many of the abnormal conditions affecting the tract, the duodenum is the great point of correlation between the upper and intermediate portions of the tract, and as such it enjoys a position of wide-spread importance as well as great potentialities for harm. The liver, pancreas, stomach, and small bowel are all intimately associated with it. No one has yet demonstrated in exactly what fashion the reciprocal relationship of the duodenum, stomach, and pancreas is carried out, although it is now generally acknowledged that the regulation of the acidity of the gastric secretion is produced by a mechanism which has its origin in the duodenum. The work of the gall-bladder is undoubtedly dominated by the chemistry of the duodenum, and the same is probably true of the external secretion of the liver. More recently Carlson and Ivy have pointed out the great importance of the duodenal or intestinal phase in the formation of the gastric secretion, studies which seem to be borne out by Garbat and others, and which I have confirmed to my own satisfaction. Into the literature of gastric physiology have penetrated the terms "intragastric" and "intraduodenal tension," terms which are certain to play an important rôle in the future study of the function of these organs. The information yielded by gastric and duo-

denal intubation on the function of these organs is already a large and increasing one, and this method of procedure represents a method in the study of gastric and duodenal pathology which is now routine.

The progress made in the study of duodenal lesions by means of the *x*-ray is also of the greatest value. In fact, the visualization of the duodenum by means of modern methods is now an accomplished fact and has revealed many of the anomalies which occur in this region. I can remember the uncertain state of roentgenologic study of duodenal conditions, more particularly ulcer, in 1911 and 1912 when the technic was not developed to the degree that it is today. I can distinctly recall Hozknecht's studies in duodenal peristalsis in 1912. He was one of the first to employ a liquid suspension rather than an opaque meal. Much of our progress is due to the use of a liquid suspension, which by means of palpatory technic can be forced into the duodenum and maintained there for an interval of time. No method equals screen study or fluoroscopy in the determination and visualization of duodenal lesions, and only prolonged practice enables the observer to acquire this technic with dexterity. In the hands of Carman and others it is developed to its greatest degree. With rapid serial pathotography it is possible to record in most instances all the important points in the demonstration of organic duodenal lesions, but the palpating hand under the fluoroscopic screen will more satisfactorily solve the problems which arise, and by repeating the procedure after the successive passage of bismuth or barium into the duodenum observes the transit of the opaque material as it courses through the duodenum.

The duodenum is as highly characteristic and also variable in its picture under the screen as is the stomach. Its form is dependent on the habitus of the individual and the nature of the surrounding organs. The picture of the duodenum with the J or fish-hook stomach is different from the highly placed duodenum seen with the steer-horn stomach, and the visualization of all parts of the duodenum in the latter is not always an easy performance. Deformities in the duodenal cap are like-

wise difficult to demonstrate in some of these cases owing to the arrangement of the organs and the difficulty in clearly visualizing the cap in all planes. The cap of the duodenum which is most easily visualized in most cases, and which after a short preliminary rest fills out admirably in the average case is undoubtedly the most susceptible portion of the duodenum for study. A sharp, well-filled, and freely movable cap is always a satisfactory finding and is usually of great importance, particularly when one suspects an ulcer of the duodenum. Inasmuch as 95 per cent. of all duodenal ulcers affect this portion, the finding of a normal cap casts in serious doubt the diagnosis. All sorts of deformities of the cap are encountered, varying from the gross deformities of duodenal ulceration to the extraduodenal deformities most often due to pericholecystitis and adhesions to the liver. Pressure defects on the cap due to a distended or dilated gall-bladder are also well known, this indirect finding being considered of importance before the more direct study of the gall-bladder by cholecystography became popular. The internist has been familiar with the typical picture of pyloric stenosis with the large stomach, the food retention, and the retention vomitus. It was only by the scalpel of the surgeon and the painstaking studies of many roentgenographers that most of these cases were shown to be not gastric but duodenal stenosis and most frequently due to obstructive duodenal ulcer. Ulcer at the pylorus is relatively rare and most gastric ulcers are more than $\frac{1}{2}$ inch away from the pylorus. The picture of benign food retention, with its gastric analysis, revealing high acid figures and hypersecretion and the large stomach, is the common one seen in benign stenosis due to an obstructing duodenal lesion.

Much more *interesting is this picture without the typical finding of an obstructing duodenal lesion in the first portion.* My attention was first seriously drawn to this possibility by the following case which illustrates the difficulties which are encountered: B. E., aged twenty-eight, had been suffering for several years with poorly defined digestive disturbances characterized principally by distress and occasionally pain shortly after eating, relieved only by vomiting and by rather obstinate

constipation. A study of her emptying stomach revealed food retention, considerable mucus, and no free HCl, her digestive response was indefinitely prolonged and characterized throughout by a very low total and no free acidity. Her blood Wassermann was negative and there was no evidence to support the belief that there was a growth. Physical examination of the abdomen was entirely negative so far as the demonstration of a

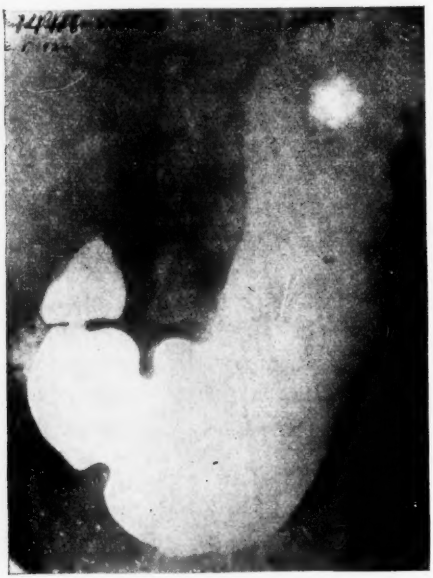

Fig. 43.—Miss B. E., showing outline of the stomach and the cap of the duodenum.

palpable mass or even localized tenderness was concerned. I studied her under the screen and she had a very large dilated stomach. No portion of the stomach showed even a suspicion of a defect. What was more striking was the fact that the bulb of the duodenum or the cap filled out readily and completely with little or no enlargement. There was nothing in the picture under the screen or in the photographs which were taken which indicated the cause of undoubted twelve-hour retention which

she presented. In studying the duodenum I was impressed with the fact that the angle between the first and the second portion was rather accentuated, but apart from this finding there was no clue to the possible cause. The duodenum on intubation revealed the same excess of mucus with a high leukocyte count and the general picture of a gastroduodenitis. Her appendical region was tender, but on my examination I was unable to visualize it. I could only make a diagnosis of gastroduodenitis,

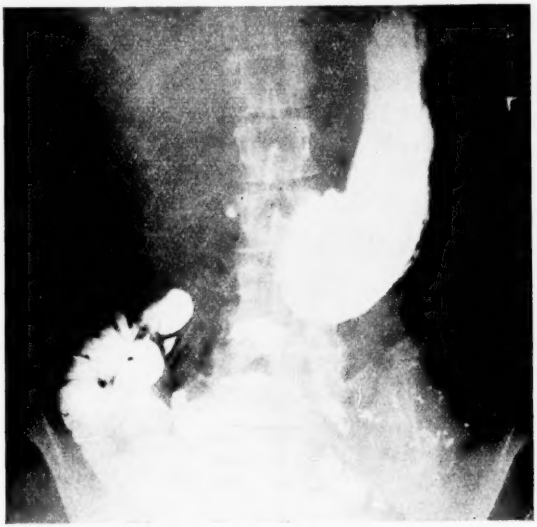

Fig. 44.—Miss B. E., six-hour retention.

possible biliary disease, owing to the richness in all the duodenal samples in leukocytes, and atonic dilatation of the stomach. Her subsequent progress was not satisfactory and I had Dr. Manges study her. He came to practically the same conclusion, with two important exceptions. He believed that the angulation between the first and second portion might be responsible for some of the dilatation, and second, he was able to visualize the appendix, which was not normal. In spite of every precaution she was not improving, and I felt that no progress would be

made until we removed the appendix and inspected the gall-bladder and duodenum. This was done by Dr. E. J. Klopp, who performed the following operation: "Transrectus incision. Gall-bladder walls decidedly thickened. Dense adhesions between it and the beginning of the second portion of the duodenum causing marked kinking of the duodenum. The adhesions were severed and the gall-bladder removed. *As the adhesions were severed the duodenum resumed its normal contour.* The appendix was full of concretions, thickened, and was removed." In this connection it might be stated that she had never had an attack of appendicitis, and this finding was incidental to the condition which was described above. Since the operation she has slowly improved. She is not entirely well, but so much better that there is no comparison between the state of toxemia, exhaustion, and distress which preceded the operation and the degree of only partial inefficiency which followed it. It is interesting to note that for more than a year after the operation gastric chemistry remained unchanged, but in the last two months there is an actual demonstrable presence of considerable free acid in the stomach. Furthermore, as was to be expected, the dimensions of the stomach have been markedly reduced.

A totally different evolution of obstruction of the second portion of the duodenum is shown by a study of the following case: In this case a careful study only two months previous to the time that I first saw him failed to reveal the presence of any organic lesion or any sign of obstruction. *Here again the whole picture was that of a classic pyloric stenosis, although the history by no means suggested this possibility.*

Mr. J. J. G., aged forty-three, suffered from gastric discomfort for the last two years. He complained of gnawing pain and discomfort more distinctly in the right hypochondrium occurring some time after meals, and relieved by milk or food, soda, or even magnesia. The pain occurred in every way similar to that of duodenal ulcer, but has been much more persistent of late. Recently he lost weight, being 7 pounds below his normal weight of a year ago. He has taken milk at frequent intervals to relieve

his distress, but in spite of the ingestion of almost 2 quarts a day and the addition of three meals, the weight loss continued. His history otherwise was of no particular interest except for the fact that he had several infected teeth which were held responsible for his condition. He had medical aid from several sources, but apparently the cause of his trouble was not clear. Two

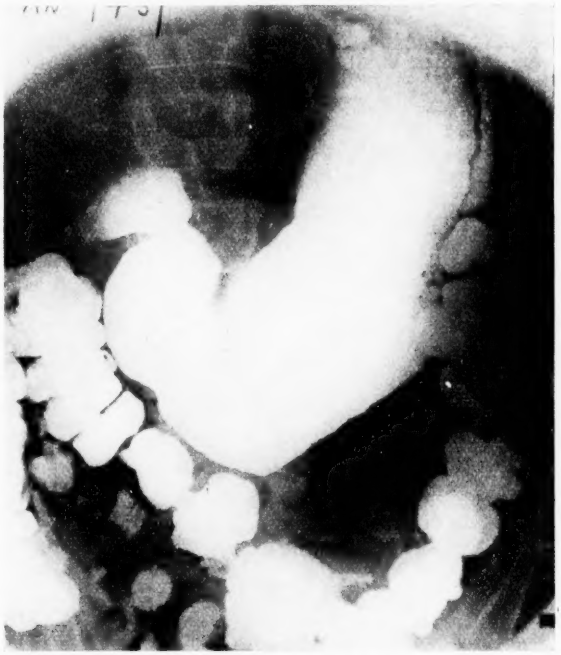

Fig. 45.—Appearance of the stomach and cap of the duodenumin Mr. J. J. G. This patient had marked stenosis just beyond the duodenal bulb.

months previous to his appearance at our office he had been carefully *x*-rayed by a thoroughly competent observer, but the report at that time indicated no trouble with the duodenum. *This is significant inasmuch as the evolution of the condition occurred rapidly after this point.* When I first saw him I remarked at the very large dilated stomach which he presented. On the first examination there was clearly retention, and I was unable

to get a clear view of the duodenum on the first study. I then had him go without breakfast and luncheon and made a preliminary screen study. He had distinct retention. I then lavaged the stomach, and only after this procedure was I able to get a satisfactory view of things, believing that the picture was characteristic of an obstructing duodenal ulcer. I was surprised

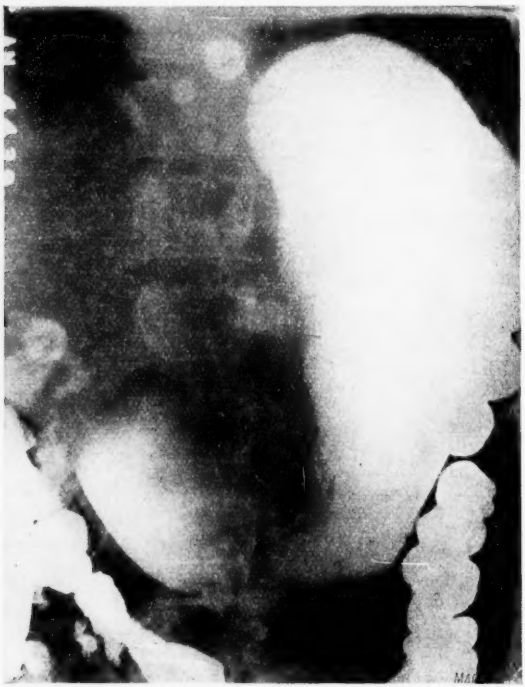

Fig. 46.—Mr. J. J. G.; notice size of the stomach in the recumbent position.

on palpation to note that I could fill up the duodenal cap perfectly and there was no sign of a defect. Just beyond the first portion, however, the duodenum was markedly narrowed down, almost filiform, and there was clearly obstruction at that point with some tenderness. My first impression was a pericholecystitis, or possibly an ulcer at that point, but I could make out

no semblance of a niche. I sent him to the hospital, had systematic lavage performed, with very considerable subjective relief, and then had another study made. His fasting stomach contents registered T. A. 82, F. A. 39 positive occult blood reaction, definite hypersecretion, and food retention, his fractional analysis showed an enormous prolongation of the digestive curve with an acidity which mounted up to 120 T. A. and a correspondingly high free acidity. Both the stools and the gastric contents were positive for occult blood. Dr. Manges then saw him and found the same state of affairs, namely, marked obstruction of the second portion of the duodenum with probable constricting adhesions, and possible ulcer. Obstruction was undoubtedly present and operation was decided upon, although the treatment he had received had undoubtedly lessened his symptoms. It is interesting to note in this connection that his pain became more persistent and there was not complete relief by lavage.

Dr. John H. Gibbon performed the operation, and his findings were as follows:

"Under m. g. o. anesthesia I opened the abdomen through the upper right rectus and found the first portion of the duodenum and pylorus quite markedly dilated. The gall-bladder and ducts were normal. The head of the pancreas was very much enlarged, densely hard, and nodular. This condition was present to some extent back to about the middle of the pancreas. There were a good many moderately enlarged glands in the mesentery of the jejunum. The duodenum was densely attached to the pancreas, but I could make out no ulcer. The diagnosis of the condition was difficult, as I did not see how a carcinoma of the head of the pancreas could produce such definite obstruction of the duodenum without affecting the common duct, and yet I was unable to find any evidence of ulcer. The patient had had none of the usual symptoms of pancreatitis. The plain indication seemed to be a posterior gastrojejunostomy, which was done."

Deformities of the first and second portion due to extra duodenal pathology are not uncommon. In fact, the gall-bladder in many instances is responsible for this finding. A not unusual

condition is the finding of reduplication of the first and second portions of the duodenum in such a way as to resemble actual diverticular formation. This must be differentiated from the condition which is described in the next case, and which I have encountered from time to time. The following was the first case that I felt justified in suggesting operation:

Mr. P. C. H., aged forty, has been suffering for the last five years with almost constant distress in the upper abdomen. At times he complained of discomfort in the lower right quadrant,

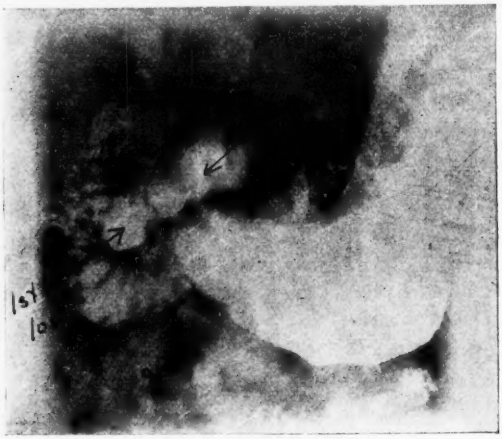

Fig. 47.—Mr. P. C. H., showing part of duodenal looping. In this picture it has the appearance of a diverticulum.

but there was no evidence to indicate that he had an actual acute attack of appendicitis. His gastric symptomatology was irregular and lacked the periodicity of ulcer, although he had been treated for presumed gastric ulcer over a considerable period of time. He had no vomiting or nausea, but sourness, heartburn and gastric distention, and distress after eating. He was engaged in a high-pressure business and was undoubtedly very "nervous." On studying this patient on the screen, the stomach was slightly enlarged. It was by no means actually dilated. Peristalsis was vigorous, but there was no antiperistalsis, and there was

no sign of a defect in the anteroposterior or lateral position under the screen. On the other hand, there was marked deformity of the first and second portions of the duodenum, with pronounced looping of the second portion, suggesting a pericholecystitis. He had been to several of the clinics in Germany and they had insisted that he had a duodenal ulcer. His gastric analysis did not suggest this possibility, it was not of the climbing type, there was no hypersecretion and food retention in the fasting stomach, only a very small back-up of bile, which did not persist during the digestive period. Gastric analytical studies clearly pointed rather to a diffuse gastroduodenitis than an ulcer. I have seen this looping on a number of occasions and always ascribed it to a diffuse inflammation in the upper right quadrant usually associated with gall-bladder inflammation. In fact, I have 6 cases at the present time, none of them operated on, where this phenomenon is present. In view of the very marked persistence of the symptoms and the fact that there was also present evidence pointing to a chronic appendix which was visible, beaded, and tender, but movable, we decided on operation. Dr. E. J. Klopp operated, with the following findings, indicating clearly the nature of the pathology.

Operation.—Kammerer incision. Gall-bladder clinically normal. Broad adhesions between it and the second portion of the duodenum, making two definite pouches of the duodenum. Bands of adhesions were separated, and as they released the duodenum assumed a practically normal shape, although it continued to be larger than normal. Pancreas was slightly harder than normal. The appendix was bound down by adhesions. These were severed and the appendix removed.

This patient was undoubtedly improved by the operation, but he still has symptoms in every way similar to but not as severe as those presented before the operation. I have screened him on several occasions since, and I am satisfied that no real obstruction occurs to gastric evacuation. He has neither six-hour retention, nor evidence of food retention on intubation, but he has "adhesion dyspepsia" and is most readily relieved by antispasmodics and sedatives.

He is the only patient within the last two years that I have operated on for this anomaly; others of this type have been treated medically by measuring gastric tolerance, regulating the diet, and controlling symptoms.

The pancreas can be responsible for deformity of the duodenum. Enlargement of the head of the pancreas can flatten out the

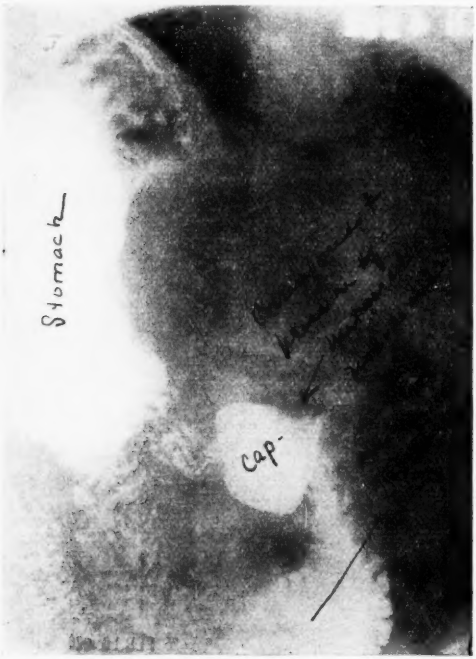

Fig. 48.—Carcinoma of the pancreas (middle portion and tail). Picture is, unfortunately, reversed, but shows the dilatation of the third portion of the duodenum seen in a case operatively demonstrated.

horseshoe of the duodenum and present one of the first signs of that disease. Equally important are the pressure defects on the gastric image which are now well known. On several occasions the only clue to pancreatic disease was the presence of one of the above changes.

An interesting case of that description recently presented itself in an individual who dated all his trouble to thanksgiving day of last year. He believed, as do most individuals with digestive disturbances, that a dietetic indiscretion was responsible for his trouble, when in most cases the dietetic indiscretion was the first signal that some organ was not functioning properly. This patient developed pain most pronounced in the left hypochondrium, and since that time up until April of this year the pain and distress were singularly resistant to treatment. The pain usually became worse at night and was accompanied by a slow progressive loss in weight. He was carefully studied in Dallas, Texas, and the only finding of any importance was a slight defect in the upper portion of the bulb of the duodenum. Our studies were equally barren with possibly two exceptions—there was unquestionably some little defect in the bulb and there was a delay in the third portion of the duodenum. Gastric studies, duodenal studies, fecal studies, blood studies, and physical examination were entirely negative. Dr. Manges, Dr. Patterson, Dr. Davis, and Dr. Nassau and myself studied him, and we felt that he had either a lesion in the first portion of the duodenum between it and the gall-bladder or a lesion of the pancreas involving the third portion.

At operation the gall-bladder was normal, but the pancreas was malignant in the middle portion and at the tail. Dr. Nassau operated on him, but there was nothing to be done, and his subsequent course has been typical of the disease. In this case nothing in the entire examination with *the single exception of the behavior of the third portion of the duodenum suggested the possibility of pancreatic disease, and even at this stage the condition had progressed to the point where several nodules were found in the liver.* In my own experience a pressure defect on the stomach is probably the most frequent roentgenologic finding. We must be on guard for the type of pancreatic carcinoma which affects the middle portion of the body or tail. This gives during a large part of its course no evidence whatever of interference with either the common bile-duct or pancreatic duct.

The deformities of the duodenum secondary to gall-bladder

diseases are many and belong to two groups, one preceding the operation and due to the distention, direct pressure effects, adhesion formation from pericholecystitis, and marked alteration in the course of the duodenum. These are best appreciated by a study of the duodenum on the screen and particularly the passage of the opaque meal through the first and second portion. A fixed duodenum, irregularity in the upper portion, angulation, an unusual course of the duodenum, so that it seems to be depressed, angulated, kinked, or twisted between the first and second portion. These are often valuable indirect signs of gall-bladder disease, particularly if the region of the gall-bladder above and outside of the duodenal shadow is sensitive to touch. For years I have studied these signs of gall-bladder disease, and even though we are depending today on the direct visualization of the organ by cholecystography, the indirect signs and particularly those which result in a permanent alteration in the duodenal transit are important to recognize. It is not my purpose in this résumé to discuss this phase of duodenal pathology. It suffices to indicate *that one of the commonest causes for malformation of the first and second portions of the duodenum is to be found in an underlying gall-bladder pathology.* When the clinician uses all the methods at his disposal, such as fluoroscopic study, duodenal intubation, and finally cholecystography, as well as the study of the feces, it is hardly likely that he will overlook many of these cases when they are sufficiently well defined.

More interesting is the duodenum after gall-bladder operations. Several years ago I remarked the very constant alterations which occurred in the duodenal cap after cholecystectomy. The findings were present even when the operation was performed under the best of conditions and by the best of surgeons. In a large proportion of cases there is fixation of the duodenum and often serious deformity. In the first 67 cases of postoperative gall-bladder cases which I studied for recurrent symptoms in the upper abdomen the majority showed evidence of duodenal deformity. Since then I have seen many more of these cases and I expect to see one out of every two cholecystectomies which give symptoms show some anomaly in the course of the duodenum.

Not all of these cases show subjective symptoms, but many of them will have at times evidence of adhesion "dyspepsia." An illustration of the extent to which duodenal deformity can progress after cholecystectomy is illustrated by the following case in which almost complete obstruction followed:

Duodenal Obstruction Secondary to Cholecystectomy.—Mrs. O. H., aged sixty-three, had a cholecystectomy performed for cholelithiasis. The operation was clean cut and uncomplicated in every way. About a year later she complained of

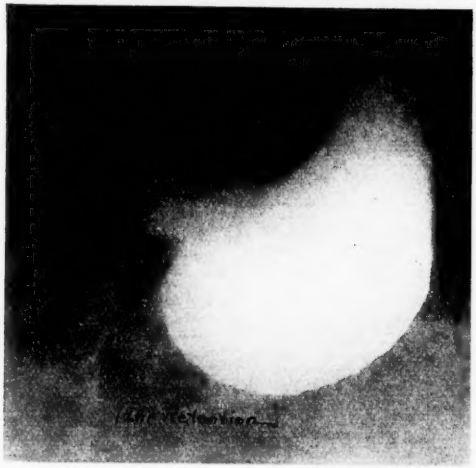

Fig. 49.—Mrs. O. H.; twelve-hour retention in simple duodenal obstruction secondary to cholecystectomy.

pain, distress and heartburn, and slight constipation. I saw her at this time and noted on the screen gastric dilatation, with increased but not reversed peristalsis, no sign of any organic defect in the gastric wall, but marked deformity and fixation of the duodenum undoubtedly due to the old operative site. There was considerable six-hour retention, and a small twelve-hour retention with the tube. I was unable to introduce the tube into the duodenum. Acidity was still intact, but there was little evi-

dence of hypersecretion and no demonstrable hyperacidity. I put her on antispasmodics, gastric lavage, and small frequent feedings, with a disappearance of all subjective symptoms. She held her weight for a time and remained apparently well. Eight months later the old symptoms returned, and on examination the stomach was distinctly dilated. There was not only twelve-hour but perceptible twenty-four-hour retention. Reversed peristalsis was clearly seen, and at intervals of three or four days retention vomiting occurred. *x*-Ray studies clearly emphasized more marked obstruction of the duodenum. I had Dr. Manges see her at that time because I felt that she could not possibly recover without operation. His report was "Very marked dilatation at the pylorus and duodenum with more than half of the barium in the stomach in six hours and an appreciable quantity of barium in twenty-four hours. There is vigorous peristalsis just as often in the reverse direction as in the right direction."

Operation was decided upon, and Dr. John H. Gibbon made a thorough exposure of the upper abdomen. The entire upper third of the duodenum was firmly adherent to the under surface of the liver and in no way was it possible by any plastic procedure to insure permanent relief. He did a posterior gastro-enterostomy, which resulted in complete and satisfactory relief to the patient. I have a letter from this patient one year later and apparently she has no difficulty of any kind. Furthermore, her food tolerance seems to be normal.

The following is an unusual case because it presents many of the difficulties inherent in duodenal diagnosis and emphasizes other angles of such a case. Mr. C. T. The following history is quoted verbatim from the report at the Johns Hopkins Hospital. It emphasizes the many peculiar manifestations shown by this patient and is a most thorough report. The details of this case are given because abdominal section revealed an extraordinary arrangement of the duodenum, which must have accounted for much of the trouble complained of by the patient. There was no other gross pathology in the abdomen.

"Admitted: January 11, 1924.

"Discharged: February 8, 1924.

"Diagnosis: Purpura hæmorrhagica(?). Secondary anemia.

"Result: Improved.

"*Complaint.*—Stomach or intestinal trouble.

"*Present Illness.*—About December 17, 1920, patient took two 'calotab' tablets to relieve constipation. The morning following patient became sick, was nauseated, vomited several times, the vomitus containing fresh blood. He had one small constipated tarry stool. He was sent to bed for three weeks

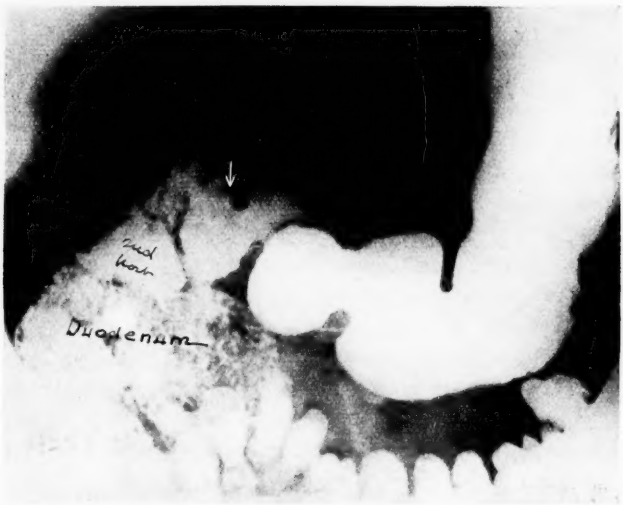

Fig. 50.—Mr. C. T.; marked duodenal deformity due to adhesion formation and deep duodenal stenosis at the duodenojejunal junction. Notice small size of stomach.

and given liquid diet. He had soft diet for next two months. There were no digestive symptoms of any kind preceding this attack. No epigastric pains, no eructation of acids, no flatulence. Two years preceding this attack were spent in Island of Guam, but patient had no tropical disease and no intestinal trouble other than perhaps one slight attack of diarrhea, which was not severe enough to cause him to consult a physician. Stool examinations were made every six months during this period, but so far as the

patient was informed his stools were always negative. The patient remained quite well from January 15, 1920, had no more tarry stools, no nausea or vomiting, no indigestion until December 20, 1922. At this time he had another tarry stool, but was not ill. An examination was made of this stool and occult blood was reported. Patient went to Dr. B. J. Lawrence, of Raleigh, N. C., who operated two weeks later for gastric ulcer after an *x*-ray examination reported a defect in the stomach. No ulcer was found, but appendix was said to contain pus and was removed. A few weeks later another tarry stool was passed. The same thing happened a few months later. In November, 1923 there was some slight indigestion, relieved by taking soda, never by eating. On December 17th patient became very faint and weak while at work. The following morning there was a tarry stool. That evening he was nauseated and vomited, but is uncertain as to presence of any blood. This weakness lasted for a few days and patient has been in bed until leaving home for admission to hospital.

"At Hopkins he was thoroughly examined, but his general physical examination was negative, and proctoscopic examination was likewise unable to explain the anemia. His blood-count was R. B. C., 2,776,000; W. B. C., 6080; Hb., 33 per cent. His stool examinations were entirely negative for parasites; blood chemistry normal, and he was transfused, with an improvement in the blood-count. Dr. Longcope believed that he presented some of the symptoms of purpura hæmorrhagica. There were also many small hemorrhages in the eye-grounds."

When I saw him I was impressed with the possibility of an infection through the upper digestive tract, possibly the biliary tract, as a cause for his symptoms. He presented all the symptoms which have already been enumerated as well as evidence of a low-grade toxemia, which was apparent, He had no gastric retention, a low curve, clean-cut evidence of a gastroduodenitis, blood in his duodenum and his stools, nothing definite on sigmoidoscopy, but when I screened him he had the most extraordinary convolution and distortion of the duodenum which I had seen for some time. I unhesitatingly made a diagnosis of

gross duodenal deformity and pathology regardless of the previous operative findings. The only question to my mind was the doubt as to whether there was an ulcer of the duodenum in the first portion. It was clearly notched, but the defect was certainly not characteristic. Furthermore, the history was totally unlike that of ulcer. I had Dr. Manges *x*-ray him after I studied him, and he was inclined to believe that there was an ulcerative lesion in the first portion. In any event, we all agreed on the manifest pathology of the duodenum and we could find no other evidence of intestinal bleeding, either on sigmoidoscopic examination or by *x*-ray study. His stomach was clearly not the source of hemorrhage. Operation was then decided on and performed by Dr. Nassau. The picture present was an unusual one. He had most marked deformity of almost the entire duodenum, with looping and distention of the coils, and the entire visible portion of the duodenum was distended where not tied down, and also distinctly redder than normal. This was in marked contrast to the successive loop of jejunum which was collapsed and distinctly paler, almost slate colored in hue.

At the operation there were wide-spread adhesions encircling the old incision. Separation of these was difficult on account of the numerous adhesions to the colon and duodenum. Careful search of the abdomen was made and at the duodenojejunal junction a large falciform membrane was found that tilted the beginning of the jejunum sharply upward. This was incised and the duodenum allowed to fall away to its normal position. *Through an opening to the right of the root of the mesentery there was an internal hernia which contained about 8 inches of small bowel. Following the release of the membraue and the reduction of the hernia, the first portion of the duodenum returned to normal size.* No other pathology was found.

The findings just described by Dr. Nassau show the condition to be due probably to the obstruction of the duodenojejunal junction, although there was adhesion pathology in the duodenum proper. The defect in the inner aspect of the cap was due to a small adhesion and there certainly was no well-marked ulcer of the duodenum. I should have liked to have seen the

duodenal mucous membrane which probably was intensely congested and probably eroded. The patient made an uneventful recovery and from last reports is very much better. What interests me most is the fact that this patient presented all the evidence of a blood dyscrasia so clearly shown from the Johns Hopkins reports, and it will be of interest to note whether the lesions found here were responsible for his condition. I shall be interested in noting the subsequent course of this patient, as I am by no means certain that there may not have been an underlying hepatic and blood dyscrasia, although the picture on the operating table was sufficient to induce marked toxemia and undoubted bleeding.

The study of the duodenum by means of the *x*-ray has afforded an insight into many conditions which have not been hitherto understood. Bilfinger discusses the question of roentgenoscopy of the duodenum. He points out that the position of the duodenum is extremely variable. In the majority of cases the first portion of the duodenum is ascending in its general direction, in others it may be horizontal, and finally it may be found to pursue a generally downward direction. He considers the inferior horizontal portion as the most stable.

Gunsett and Weigel discuss serial roentgenography and point out the value of this method. In the majority of cases 4 to 5 films suffice to show the cap. They point out the fact that at times ventral decubitis and right semilateral decubitus are often better positions for examination. They also subscribe to the method described by Chaoul in 1918, whereby roentgenoscopic control is obtained underneath the patient by means of a mirror.

In some cases there is an unusual enlargement of the bulb of the duodenum. I have often seen this phenomenon in severe visceroptosis, and the term "megaduodenum" has been applied to those forms of enlarged duodenum neither paralytic nor due to mechanical block. Duval discusses this condition and points out the fact that in many of these cases the enlarged duodenum is, in reality, due to some form of stricture. True megaduodenum is analogous to megacolon, mega-esophagus, and other dilatations of the type occurring in different parts of the tract. I have on

many occasions seen simply enlargement of the first portion with no evidence of stenosis associated with an atonic stomach. A congenital loosening of the upper part of the duodenum associated with undue mobility of the duodenum is called "duodenum mobile" by Miyake. To those who are accustomed to screen these cases routinely this is likewise a not uncommon finding in visceroptotics. Miyake finds a series of clinical conditions which are induced by this finding. The tug of the full stomach and loosened duodenum produces traction or kinking of the common duct, with resulting stasis and sometimes infection. At times attacks of colic are induced resembling biliary colic. These patients complain of fulness, pyrosis, eructation and dyspepsia, and often manifest symptoms similar to those seen in cholelithiasis. He points out cases where operation was performed for supposed cholelithiasis, and this condition was found. In some cases icterus may occur. I have seen cases of this description in which the entire half of the duodenum was freely movable. In some of these cases there is a bile back-up into the stomach with a large amount of bilious hypersecretory fluid. These patients are prone to migraine. Miyake mentions duodenopexy as producing brilliant results, but I have never reached the point where I insisted on a procedure of that kind for relief.

Chronic stenosis of the duodenum is not uncommon. Ratkoczi points out that prior to the *x*-ray era, duodenal stenoses were confused with pyloric stenosis. This author divides chronic duodenal stenosis into two groups—one persistent and the other intermittent stenosis. In persistent stenosis the contrast material trickles constantly through the duodenojejunal junction, but only in a thin stream. In this form almost the entire duodenum is filled, and also kept filled from above. Not infrequently violent antiperistalsis may drive material back toward the bulb or even into the stomach.

There is usually gastric delay which at times may be very pronounced. Adhesions, tumors, glandular masses, in fact, anything that produces persistent obstruction will produce this condition. Intermittent stenosis is different and is recognized by the fact that the duodenum fills up almost completely, may ex-

hibit reverse peristalsis, and gives the appearance of obstruction up to the duodenojejunal junction that may persist for a variable length of time, after which the duodenojejunal junction suddenly opens and the contrast stream pours out in a thick mass into the jejunum. Causes of intermittent stenoses enumerated by Ratkoczi include movable tumors, pressure of the mesentery or superior mesenteric artery, and reflex spasm resulting from a lesion elsewhere in the digestive tract.

Barling attributes most cases to congenital anomalies, neighboring inflammations or growths, kinking or direct pressure by the mesenteric vessels. The symptoms are those of a chronic digestive disturbance with acute exacerbations of epigastric pain, vomiting, and distention. McKenty in discussing chronic duodenal stenosis likewise limits his discussion to that type. He considers the drag of the mesentery of the small bowel by a loose cecum prolapsed into the pelvis as by far the most common cause. Certainly this combination is a very common one from a radiologic standpoint. He demonstrates the effect of this drag at operation by placing the finger behind the superior mesenteric artery and observing the effect of elevating and depressing the cecum. In many of this author's cases this test was positive. Griffith points out the fact that duodenal dilatation is often the concealed cause of trouble when pathology is anticipated elsewhere and not found. He enumerates discomfort after eating, flatulence, and poor appetite as common symptoms. He furthermore points out that temporary improvement can often be obtained by selective diet, postural treatment, bowel regulation, and gastric lavage where gastric distention is present. Permanent relief is only obtained by duodenojejunostomy.

Melchior points out that the classical symptom of deep duodenal stenosis is the habitual reflux of bile or duodenal contents into the stomach. This subject is a large one and it was not my purpose to discuss this point, with this exception, that in all cases where there is a large heavily bile-tinged fasting residuum it is well to consider the possibility of some form of duodenal stenosis or some anomaly in the duodenum by which the transit of material through the organ is impaired. In almost all of those cases

mentioned above this symptom in varying degrees was present, although in some cases of extensive duodenal deformity it may be lacking.

Occasional duodenal diverticula are found. These are relatively rare and are to be distinguished from the gross malformations involving the entire lumen mentioned above. Recently I found a duodenal diverticulum between the first and second portion projecting into the pancreas. On several occasions I have seen small diverticula in the duodenum. Ochnell enumerates 34 cases of duodenal diverticula diagnosed by Roentgen examination. Pain was reported in 85 per cent., epigastric symptoms in 66 per cent., vomiting and acid eructations in 44 per cent. Among the associated conditions were ulcer, pancreatic, and gall-bladder conditions. They may cause, according to this author, retention in the stomach and duodenum. Twenty of this author's cases were in women, and 14 in men. The average was over fifty years. This author points out that it may serve as a focus for lessened resistance and may complicate diseases in the upper abdomen. Owing to the fact that duodenal diverticula are often buried in the pancreas, they present considerable difficulty in removal.

SUMMARY

1. Clinicians are liable to concentrate on gastric pathology to the exclusion of possible underlying duodenal pathology.

2. Instances are recorded where the picture of pyloric stenosis was perfectly mimicked by an obstructive lesion beyond the pylorus.

3. Apart from the well-known form of chronic obstruction due to a stenosing duodenal ulcer, there are many forms of duodenal pathology capable of presenting a similar picture.

4. Emphasis is laid on the fact that a perfectly normal gastric contour and a perfectly uniform duodenal bulb does not exclude the possibility of a lesion beyond that point.

5. The finding of a large fasting residuum which is heavily bile tinged is suspicious of a lesion of an obstructive nature beyond the pylorus. A bile-colored residuum has no particular

significance, inasmuch as practically one-half of the normal residual which are removed show traces of bile. An unusually large residuum with marked bile reflux is, however, suspicious of organic duodenal pathology.

6. The modern *x*-ray procedures enable us to visualize and trace the entire course of the duodenum without the recourse to intubation.

7. Evidence of pancreatic disease may be presented by anomalies and deformities in the course of the duodenum.

8. The indirect duodenal signs of gall-bladder disease ought not to be overlooked in studying these patients.

9. A study of the duodenum will explain many obscure gastric cases.

BIBLIOGRAPHY

Bilfinger: Fortschr. a. d. Geb. d. Röntgenstr., Hamburg, 31, 462, January, 1924.
Gunsett and Weigel: Jour. de Radiol. et d' electrol., Paris, 8, 1, January, 1924.
Duval: Arch. d. mal. de l'app. dig., etc., Paris, 14, 197, March, 1924.
Ratkoczi: Amer. Jour. Radiology, 12, 246, September, 1924.
Barling: Brit. Jour. Surg., 10, 501, April, 1923.
Melchior: Arch. f. Chir., Berlin, 129, 778, June 20, 1924.
McKenty: Surg., Gynec., and Obst., 38, 444, April, 1924.
Ochnell: Arch. f. Verdauungskr., Berl'n, 31, 127, May, 1923.

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THE VALUE OF PAIN AND CERTAIN REFLEX PHENOMENA IN DIAGNOSIS

I WILL not pretend to submit anything new. My desire is to elicit your interest in a method of clinical approach which will enhance the diagnostic ability of anyone who chooses to cultivate the necessary technic. There is no intent to disparage the value of the laboratory as an aid to diagnosis. As a matter of fact, it is always important, and occasionally indispensable. You will probably agree with me, however, that there is a growing tendency to lean too heavily toward the laboratory side of diagnosis. In the abstract the findings of the laboratory often may be of very little value. They become of particular value only when they are correlated with the history and physical findings of the patient who is being studied. Then, too, their true evaluation presupposes a certain degree of familiarity with laboratory work in general, particularly with normal standards, which many physicians and surgeons do not possess. Sensible as we may be of the value of the advances in biochemistry and the more recent field of physical chemistry, there are few who possess a knowledge of body chemistry in its relation to end-products sufficient to serve as a working basis. Still fewer who grasp the significance of proteins as ampholytes, or appreciate their electric phenomena or stoichiometric properties, or understand Donnen's membrane equilibrium in its application to the cell, or the importance of dissociation and ionization to an understanding of *p*H. Yet, all of these and many more fundamental principles are essential in an attempt to understand the normal and morbid physiology of the cell as they are being revealed today. Perhaps the hospital intern best exemplifies the attitude of many of us. He takes a

history, often perfunctorily, makes a physical examination, frequently lacking in details, then asks for all of the laboratory work which the facilities of the institution afford. His working diagnosis, when he makes any, is then based on the laboratory findings. He thus loses sight of the great value attendant upon a careful history; the opportunity afforded to study the psychic phase of the patient, when, with defenses down, so to speak, the patient is concentrated on answering questions. Nor does he sufficiently cultivate his powers of observation when he makes his examination, because, as is increasingly evident, he depends more and more upon the laboratory. The surgeon, on the other hand, with an attitude of self-sufficiency which unconsciously grows upon him, due probably to the mechanistic character of his work, resorts too infrequently to even the simple forms of laboratory diagnosis.

If one reviews the rather long list of eponymic diseases or of eponyms in a narrower sense, he will be struck by the fact that we are indebted to those splendid clinicians of Great Britian especially, men of well-trained, scholarly type, who have been practising physicians, doctors in the best sense of that much maligned word. They were careful bedside observers, and were forced to exercise their unaided senses, for the laboratory phase of diagnosis had not been developed. A perusal of their contributions to medicine leads to the conviction that we are insensibly drawing away from the older methods which have served so well. It is not possible for a busy family practitioner, particularly when away from the larger centers, to avail himself fully of the laboratory. He must learn to depend upon his unaided senses except for the simpler laboratory procedures; his busy life may even afford insufficient time for these.

My appeal, then, is made to that great majority of doctors whose daily routine is one of direct service, whose lives are intimately associated with the family. If it were the custom to keep careful notes and to faithfully study and record all observations, as to occupation, weight, diet, and habits of his patients and the family, we should be put into possession of a most invaluable record of the natural history of disease.

In the higher forms of animal life, pain as a defensive mechanism, and its attendant reflexes, are phenomena of inestimable value in diagnosis. This implies a complex and highly developed organism, but in principle it is similar to that met with in more lowly forms. Parker[1] describes it well when he speaks of a reflex arc as consisting of a receptor, adjustor, and effector system. In the most primitive forms the effector element is the first to appear. This is really a muscular tissue, an effector system, as seen in the sponges, and perhaps to the best advantage in Stylotella. Of course, even in the protozoa and the protista of Haeckel, response to appropriate stimuli is perfectly evident, but the first evidence of a structure approaching a neuromuscular, or at least a muscular system, is seen in the sponges. Here response is slow, but definite. This neuroid response is purely muscular, and can be easily demonstrated in the contraction of the finger-like processes and the sphincter contraction of the oscula. No nerve-fibers have been found. Even in the vertebrates a similar effector system exists, in some as an early manifestation, in others as a permanent mechanism, and even in man an effector has been demonstrated, though the part is also under nervous control. This is equally true of some of the most lowly forms. In the chick the heart develops at about the twenty-third hour of incubation and begins to pulsate six hours later. At this stage the neural crests have not formed and the neuroblasts are undifferentiated. It is not until some days later that nerve tissue becomes a part of the mechanism. Cultures made *in vitro* from the chick heart prior to the development of nervous tissue will, in many instances, pulsate, showing even a more definite effector system than is seen in the sponges. The frog embryo heart, freed from all nervous connections, will also continue to pulsate when removed from the body. Whatever be the ultimate mechanism, it is certain that myogenic action precedes neurogenic.

The nerve-cells found by Remak[2] in the heart muscle may modify its action, but it must be evident when individual muscle cells may be seen to pulsate, as they do in embryo chick cultures of heart tissue, that primitive contraction is myogenic. A further connecting link can be studied in one of the tunicates, the

molgula. Here the heart consists of a swollen portion of a tube, one end of which runs to the viscera, the other to the gills. I have watched this for long periods in the course of some work I was doing at the Marine Biological Laboratory at Woods Hole, Mass. Its peculiar interest lies partly in the periodic reversal of its heart beat, and partly in the finding of nerve-cells at each pole of the heart from which contraction begins. For a few moments pulsations will flow to the visceral end, then a sudden reversal, and pulsations flow to the gill end. It is questionable whether these nerve-cells have anything to do with the rhythm, for though the organ is small, isolated portions of it pulsate independently, hence another evidence of a pure effector system. Smooth muscle-fibers of the chick amnion are also effectors, for they continue to pulsate in tissue cultures. The sphincter of the iris of a number of vertebrates, including man, though under nerve control, can be wholly bereft of nerve connections and be shown to act as a simple effector. Small groups of smooth muscle-fibers teased out from the sphincter may be made to contract by a fine beam of strong light. This has been shown to be due to contraction of the pigmented, smooth muscle-cells of the sphincters which absorb the short light waves. In the Fundulus, especially, it is a simple matter to study the pigmented cells of the skin, the chromatophores. They, too, are probably muscle-cells, yellow and black, xanthophores and melanophores. This fish changes its tint according to the degree of light exposure, as does the squid, and also whether it is placed upon a dark or light background. Here, however, if one cuts a certain nerve-fiber in the posterior third of the Fundulus, this function is lost. The sea anemone affords an interesting opportunity to study the relationship between the receptor and effector systems, especially in relation to the acontial muscles of the filaments and the peristaltic action of the circular muscles of its cylindrical body. Even of more interest in its bearing upon fibrillation, as seen in the human heart muscle, is the so-called "trapped wave" which can be produced in the Hydrozoa and Scyphozoa, the jelly fishes. In them an initial impulse originates in a marginal body and spreads by way of a nerve net over the

umbrella of the animal. By appropriate sectioning a wave may be made to pass by a circuitous route, trapped as it were, somewhat analogous to the circus movements used by Garrey[3] and Mines[4] to explain the action of the fibrillating muscle in auricular fibrillation. The elemental forms of response then are muscular and ciliary, both effector systems, lacking nerve control.

Next we meet a receptor and effector system as exemplified in the sea anemones and jelly fishes. Here the nerve net is seen to advantage, as it is in relation to the heart and blood-vessels of vertebrates, including man, and likewise in the Meissner and Auerbach plexuses of the intestine. All such structures have in common a remarkable degree of autonomy, and in many instances a definite polarity, as shown especially in the nerve net of the intestinal wall.

Thus far we have said nothing as to the appearance of adjustors and synapses in this brief description of the development of a neuromuscular system. It is timely, however, to point out that a form of diffuse transmission, a fan-like wave, is characteristic of the nerve net, and polarity of transmission is characteristic of a higher or synaptic form. In these gradations the receptor cells, always of epithelial origin with all parts of the nerve structures, at first directly epithelial or subepithelial, gradually come to occupy a deeper position in higher forms of life, as the connecting fibers multiply and divide, at first by a process of delamination, and finally, by natural involution of the epithelial portion, to form a neural crest from which the ultimate nervous tissue develops. Hence, the receptor, at first superficial, now becomes the deepest part from which the fibers spread, other receptors arising as connecting links between nerve systems, collaterals forming in the central ones, synapses, and the whole correlated by an adjustor system, a primitive cord in the earlier phases and a brain in still higher forms. The function of the synapse seems to be to strictly polarize an impulse, *i. e.*, to permit it to pass only in one direction. It is the most important development in the gradation from simple effector system to the complex central system, with its receptors, effectors, adjustors, and synapses. It is evident that the infinite varieties of sizes

and shapes of animal bodies, their increasing complexity as we ascend the scale, the increasing need for some defensive mechanism, mechanical, physiologic, and finally psychic, brings about increasing separation of receptors and effectors, their subdivision into special functional types, and an eventual adjustor which governs the whole directly or reflexly. No apology then is necessary for the time consumed in a brief attempt, disjointed and incomplete, necessarily, to evoke a greater interest in the part played by the neuromuscular apparatus in a comparative sense, from the simple to the complex. In some of the lower animal forms, and in the primitive vertebrates, the amphioxus, there is a segmental arrangement of the nervous system. With added complexity of form, with the development of a brain and limbs, this character of distribution is lost to a greater or less degree. The development of collaterals, synapses, and a sympathetic nervous system further add to the complexity from an anatomic standpoint, but fortunately, in a clinical sense, it is possible to evaluate certain sensory and motor phenomena and to utilize them diagnostically.

It was Ross[5] who first called attention to the nature of sensory disorders in visceral disease. He regarded pain as of two kinds—splanchnic and somatic. Splanchnic because he believed it was referred by the brain to the site of a lesion in an organ, and somatic because the pain may be referred to definite areas in the body wall. Sherrington[6] was the first to present a physiologic demonstration of the function of afferent sympathetic nerves. He cut and stimulated the central ends of some of the visceral nerves and found that the abdominal muscles contracted in a definite manner. This contraction should be regarded as heightened tone, and it is this tonus, with or without pain, which constitutes the essential factor in the diagnosis of a number of symptom complexes. Tonus is not the same in all muscles, however. For instances: stimulation of a cerebrospinal nerve to a long muscle, or a neural discharge to such a muscle, causes contraction of the entire muscle. In the case of the flat muscles, however, contraction is rather of the massed, fibrillary type. Small areas contract rather than the muscle en masse. This is

especially true where such flat muscles are reflexly stimulated by impulses set in motion from the viscera, transmitted by way of the sympathetic nervous system. Striated muscle everywhere receives motor fibers from the medullated cerebrospinal nerves, but it was Tchiriev who, in 1879, discovered that they also receive terminals from non-medullated fibers. Boeke suggested that these non-medullated fibers are sympathetic or autonomic, and only within the past few years these have been traced to the vertebral sympathetic ganglia. This fact later led to the view that the tone of the muscles depends on two factors—the somatic or cerebrospinal supply and the sympathetic innervation. A study of the decerebrate animal by Sherrington and others led to the discovery of both plastic and contractile tone dependent upon these two types of innervation. It was this which led Dr. Royal and the late Dr. John I. Hunter[7] to study the whole question from the standpoint of cases of spastic paralysis. After much experimental work and painstaking anatomic and physiologic study, they devised the operation of sectioning the sympathetic cord, thus eliminating plastic tone, the somatic or contractile tone remaining. Of more immediate diagnostic interest to the clinician is the fact that certain morbid conditions within the thorax may give rise to abdominal symptoms. So may certain thoracic cord lesions or lymphadenopathies or aneurysms or new growths, making pressure on nerve roots or trunks, or, as a result of bone erosion or metastasis, involving the dorsal cord or coverings.

Within the abdomen, the viscera, bereft of sensory nerves, make known their abnormal state in a purely reflex manner. The abdominal wall is supplied by the anterior branches of the lower six intercostal nerves. The necessary seat, therefore, of lesions within the cord or encroaching upon it, or upon the roots, or of lesions within the thorax capable of causing abdominal symptoms, becomes clear from the anatomic standpoint. In the case of locomotor ataxia this has a double significance. Abdominal pain in tabes is universally recognized, yet it has not always been kept in mind sufficiently, for abdominal exploration is still performed in cases in which insufficient care has

been exercised in diagnosis. On the other hand, appendicitis and peritonitis from various causes, or any usually painful abdominal condition, may run its course, and perhaps be overlooked in tabes, because of the fact that the normal neural impulses are blocked when the posterior columns of the cord are diseased. The determination of the presence or absence of pallesthesia (vibratory sensibility) in such a case would suffice to establish a diagnosis. Or, in cases with associated lumbar cord involvement, the absence of pain in dilation of the anal sphincter, a usual phenomenon in most cases of locomotor ataxia.

Jacob Hilton,[8] in his book on "Rest and Pain," was probably the first to call attention to the relation between thoracic disease and abdominal symptoms. Despite the lapse of many years, the lesson does not seem to have been thoroughly learned. I saw the abdomen opened in a case of suspected gall-bladder disease. No abdominal abnormality was found other than what seemed to be an enlarged liver. At the necropsy an extensive pericarditis with exudate was found.

Pain in the neck and occasionally in the thigh in diaphragmatic pleurisy, the wide-spread, reflex phenomena of angina pectoris, including cranial nerve involvement and extrapectoral manifestations, those also excited by inflammation of the parietal pleura, pericardium, and to a less extent, even by involvement of the heart muscle, are all of interest anatomically and of value diagnostically. It would consume too much time, however, to consider them in detail. It is rather with some of the signs evoked by certain morbid states of the urinary tract, abdominal, and pelvic organs to which I shall direct your attention. They are well known. Only the fact that they seem not to be utilized in diagnosis to the extent that they deserve is my excuse for dwelling upon them.

The late James Mackenzie[9] said, "On account of the frailty of the human mind a certain satisfaction is given when a name of some sonorousness is applied to a malady. Mental effort is hard work, and painstaking inquiry into the nature of symptoms may be shirked by the use of some fine name that seems to embrace the case under consideration."

This is well exemplified by the loose employment of the words rheumatism, neuritis, grip, and neurasthenia. On the other hand, to withhold a diagnosis until some structural change makes itself clearly evident is tantamount to a loss of interest in the face of the inevitable. Functional disturbances may also be difficult of interpretation. The symptoms resulting may be remote from, and without apparent connection with, the organ primarily involved.

We are by no means a unit as to whether the symptoms of angina pectoris are due to involvement of the heart muscle or to involvement of the aorta. If we espouse the former, how can we reconcile anatomically those cases with extrapectoral phenomena? Vomiting by no means implies a gastric origin, nor do quantitative changes in hydrochloric acid and ferments. Health means harmonious action of the entire economy. Conversely, ill health means dysharmony. The first evidence of a departure from health may be psychic; some change in disposition, or an increasing consciousness of some part, varying from mere discomfort to actual pain. In various ways, and increasingly evident to those who direct attention to an evaluation of its manifestations, the nervous system plays a part in the majority if not in all the morbid entities with which the physician is called upon to deal.

As expressed by Tilney and Riley,[10] "Every phenomenon of human life is to some degree regulated by the nervous system, and there are few diseases which do not manifest defects in its controlling influences." Anatomic diagnosis, then, is quite as important to the physician as it is to the surgeon, but less in a morphologic sense than dynamically, with a view to an attempt to reason over the phenomena presented.

Pain and paresthesia may be wholly cerebrospinal in origin, or partly sympathetic and cerebrospinal. The character and degree of sensitivity varies with the region involved and with the nature of the stimulus. Without attempting too much detail, these are grouped under two main heads: (*a*) tactile sensibility or thigmesthesia, (*b*) deep sensibility or bathesthesia. Definite common sensation is spoken of as epicritic, while the more

vague and diffuse type is called protopathic. Special sense phenomena are also epicritic. It has been found that wherever a tissue is directly sensitive, its nerve supply is cerebrospinal. Where a part is not sensitive or only indirectly so, its source is found to be in the autonomic nervous system. In either case appropriate stimuli may result in sensory disturbance of some kind, also under such circumstances, in heightened muscle tone. The abdominal viscera, kidneys, ureters, and part of the urinary bladder and female generative organs are devoid of sensory fibers. Normally their functions are performed without arresting conscious notice. Their afferent path is by way of the sympathetic to the cord and brain, thus stimulating the various cerebrospinal centers, bringing about sensory motor and sometimes glandular activity, but lacking the keen sense of position which occurs only when the reflex is primarily cerebrospinal. The receptors for these impressions are spoken of as (*a*) exteroceptors, when in the ectoderm; (*b*) proprioceptors, in the mesoderm, in relation to muscles, bones, and joints, and (*c*) interoceptors, in the entoderm, related to the viscera.

The parenchyma of glandular organs as the kidneys and liver and the parenchyma of the spleen are unable to awake any appreciable response. Those organs provided with involuntary muscle, as the stomach, intestine, urinary bladder, uterus, ducts, etc., are all capable of giving rise to sensory motor phenomena of more or less definite character, especially the hollow viscera, the stomach and bowel, ureters, and bile-ducts. Someone has said that the progress of medicine is only "a succession of forgotten theories." This is brought to mind by the fact it was in the eighteenth century that Albrecht von Haller demonstrated the insensibility of the viscera. The visceral peritoneum is also insensitive. The parietal peritoneum becomes sensitive only through its intimate relation with the preperitoneal layer of Ranström, the terminals of the anterior branches of the lower six intercostal nerves. The sole part of the peritoneum which is directly sensitive is the tunica vaginalis testis, which receives a twig from the genital branch of the genitocrural nerve, from the first and second lumbar. The ureters also have a

lumbar representation by way of sympathetic plexuses. The scrotum, on the other hand, is supplied by sacral nerves, hence it it is not tender in cases of renal colic. Developmentally, the ureter and testicle are related to the kidney and the nerve association remains, though their ultimate anatomic positions become remote. These facts we avail ourselves of in the diagnosis of renal colic. The cremaster muscle is innervated by the genitocrural nerve and the quadratus lumborum by the first three or four lumbar nerves. Hence we have the anatomic setting. In evaluating reflexes of this character the phenomena to be elicited are: hyperesthesia, hyperalgesia, and increased tension of the muscle, in direct proportion to the degree of irritation and exaltation of the particular spinal center or centers. When the original stimulus is severe, adjacent segments of the cord may become involved through the intersegmental collaterals, and thus a wider surface expression. So, too, when the exciting cause ceases to function for any reason, symptoms may remain for a day or even for several days, the cord center having become the seat of an exalted irritability. This is well seen after an attack of angina pectoris, where widely separated muscle areas may remain tender and more or less tense for some time.

The anatomic differences between the male and female as to testicle, ovary, and cremaster muscle should be borne in mind in a case of suspected renal colic. A woman admitted to the Samaritan Hospital was seen in consultation with Doctor Ruff. She complained of a dull pain in the right flank, slight nausea and flushing, with an occasional tendency to sweating at such times. She was found to manifest tenderness and tension of the lower third of the right quadratus lumborum, most marked over the crest of the ilium. She had never had colic or abnormal urinary phenomena. A tentative diagnosis of right-sided ureteral calculus was made on anatomic grounds, and further confirmed by finding of blood in the urine. Two days later she had an attack of renal colic, so called, and passed a stone a few hours later. In a male the more fleshy cremaster muscle and the tunica vaginalis testis would have given rise to even more definite phenomena. The failure of the *x*-ray to reveal the stone in

many of these cases adds to the value of the anatomic diagnosis. Posture and gait may both be changed in certain cases as a result of exalted reflexes. Effort may further heighten these, hence volitional movements may be increasingly hindered and restricted during the day, to become less marked after a night's rest. This is equally well recognized in certain diseases of the central nervous system, especially in cord lesions. Whether the urinary bladder has a double origin in the allantois and cloaca, or only develops from the cloaca, is of less importance to us in a clinical sense than its nerve supply. This is derived from the upper lumbar nerves through the hypogastric plexus and from the third and fourth sacral nerves. The former supply the upper part of the bladder. Sensory disturbances are more vague and of a diffuse, protopathic character when the bladder is distended, or when the upper portion is involved. When the base is involved, as in cystitis or in calculous disease, the sensory phenomena registered are more definite, more epicritic in character, and decidedly more acute. It is this relation, too, which explains the sphincter spasm and necessary catheterization when the skin is included in the stitch areas in perineal repair.

Time is not given to follow in detail the reflex phenomena arising in connection with the ailmentary tract, nor with the less definite but appreciable manifestations of an enlarged liver due to broken cardiac compensation. Two illustrative cases must suffice, with a brief concluding reference dealing with the gall-bladder and ducts.

A patient was seen who had been seized a short time before with violent pain in the upper abdomen. Temperature normal, but rose in the next few hours to 93.3° F., and pulse rose from 80 to 96. Two attacks of vomiting failed to bring relief. A crouching posture, with thighs flexed, made an abdominal examination difficult and unsatisfactory. It did reveal, however, intense rigidity of the entire width of the abdomen above the transverse umbilical line. The extent and character of reflex betokened the violence of the exciting factor. This, with the entire absence of a phrenic reflex in the distribution of the cervicals, led to the opinion that we were dealing with a ruptured duodenal ulcer

rather than with involvement of the biliary tract. Operation was promptly performed and the opinion confirmed. Relative uneventful recovery followed.

The second patient, a woman, was seen with Dr. J. M. Cunningham. Shortly before she had been studied from the *x*-ray standpoint. Many plates had been made and some laboratory work done. A diagnosis of visceroptosis and neurasthenia was made. An abdominal support was ordered, with the advice to follow a hygienic régime and not to dwell upon her condition. Briefly, the facts are that she had had a child; some time later she developed abdominal discomfort and pain. An exploratory operation was performed, at which time the vermiform appendix was removed. Later she developed some pelvic condition, nature unknown, but she said she was drained per vaginam. She subsequently became unable to carry pregnancy to term, developed severe backache in the lumbosacral region, extending into the thighs, toward the end of the day. To these symptoms were later added more acute ones. Pain across the abdomen from side to side, at about the transverse umbilical line, colicky in character, and eventual attacks of nausea and vomiting and marked loss of flesh. She had a marked visceroptosis. Auscultation of the abdomen revealed active peristalsis which could be seen and felt in various positions. A careful consideration of the history and reflex phenomena led to the diagnosis of abdominal adhesions binding the terminal portion of the ileum to the uterus. Operation was regarded as imperative. This was performed by Dr. Babcock, who found adhesions of such a dense character, and the ileum so angulated, that it was necessary to remove about 5 inches of it. The adhesions were between a place on the ileum, about 8 or 10 inches from the ileocecal valve, and the fundus of the uterus. The reflex phenomena were of distinct value, therefore, in locating the probable position of the lesion.

Anatomically, in the majority of cases renal colic, gall-stone colic, appendicitis, and, in fact, most of the acute abdominal lesions have fairly definite reflex criteria. (The urinary tract symptoms are spoken of as abdominal as a matter of convenience.) The essential factors necessary in their interpretation are: a

carefully detailed history, chronologically arranged when possible, and painstaking application of what knowledge we possess of anatomy, physiology, and physical signs. As to physical diagnosis, inspection first, then auscultation, followed by very light palpation and percussion. The hands must be warm to avoid the confusion of induced defensive reflexes. Only as a final procedure should deep palpation be practised. Exalted spinal centers are capable of evoking a form of phantom tumor. In tabes and in many other conditions this may occur. Neural impulses may continue to flow for some time after a stimulus, given a heightened center, and so a muscle mass may come to be misinterpreted. When in the abdominal wall it may be, and often has been, regarded as an intra-abdominal tumor.

In concluding, may I repeat that nothing new has been submitted. With equal truth it may be added that no topic has been dealt with exhaustively. Merely an attempt by suggestion to invite an interest in the application of one's fundamental knowledge in the making of a diagnosis.

BIBLIOGRAPHY

1. Parker: The Elementary Nervous System. (The writer is indebted to this monograph for many of the references in his article.)
2. Remak, quoted from Parker.
3. Garrey, W. E.: Physiological Reviews, 1924, iv, 215–250.
4. Mines, G. R.: Trans. Royal Soc. of Canada, 1914, Ser. 3, viii, 43–52.
5. Ross, quoted from Mackenzie: The Interpretation of Symptoms.
6. Sherrington, quoted from Mackenzie: Ibid.
7. Hunter, John I.: The Relationship of the Sympathetic Innervation to the Tone of Skeletal Muscle, Amer. Jour. Med. Sci., October, 1925, clxx, 469–480.
8. Hilton: Lectures on Rest and Pain.
9. Mackenzie, James: The Interpretation of Symptoms.
10. Tilney and Riley: Forms and Functions of the Nervous System.